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Introductory Training Course:

Pesticides and Public Health

1971

ENVIRONMENTAL PROTECTION AGENCY
PESTICIDES OFFICE
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FOREWORD

This study book is made available to students enrolled in the Introductory Course in PESTICIDES AND PUBLIC HEALTH to serve as a training aid and guide in their search for knowledge and understanding of concepts and technological considerations pertaining to pesticides. Such are important in developing and maintaining effective programs in the fields of environmental health and environmental protection. Since it is proper to assume that students in an introductory course do not have a strong background in the subject based either on study or experience, the reader should not be surprised to find that the authors have taken great care to explain the fundamental elements of their topics.

For the most part these papers were prepared especially for inclusion in this study book. However, it should not be considered a citable source. Any original research data contained in these papers will soon be published by the authors in another form in refereed scientific journals. Should you be unable to locate the appropriate citable reference for these data in the future, we ask that you contact the author directly.

We take this opportunity to express our appreciation to the authors for their assistance with this training course and to wish you the students rapid progress toward our common goal of adequate protection of human health and of the environment.

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May 1971

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CHEMICALS IN THE ENVIRONMENT

Frank S. Lisella, Ph.D.

Until a few years ago, the words "environment" and "ecology" were almost exclusively reserved for the scientist's vocabulary. In recent years, however, this trend has shifted and both the terms and interest in environmental-ecologic relationships have become of considerable interest. Much of this interest is probably due to the significant strides in medical science which have greatly altered the spectrum of conditions affecting the life and well-being of man. For example, the past 25 years have been characterized by marked advancements in the control of poliomyelitis, tuberculosis, diphtheria, malaria, yellow fever, and numerous other diseases. As early as 1953, it was estimated that at least 5 million lives had been saved and 100 million illnesses prevented through the use of DDT for controlling malaria, typhus, dysentery, and other arthropod-borne diseases (1). Advances such as those which were responsible for the decline of these diseases have displayed their impact upon society with mixed blessings. Thus, there has been a definite shift in environmental hazards from those with a microbial etiology to those of a chemical nature. Thousands of different kinds and combinations of gases, solids and liquids can, and do, pose potential health hazards to any, or all, segments of the public. For instance, the same technological advances which are responsible for increases in the productivity of farmland through the systematic application of pesticides may in turn create problems of a public health nature. Among these problems are the potential threats to the ecosystem, the hazards created by virtue of occupational exposure through the formulation and application of pesticides, and the possible health effects precipitated by chronic exposure to these chemicals.

The potential hazards to man from association with chemical agents need not be as subtle as the example cited. Rather, it should be pointed out that the home and occupational environments abound with chemicals which are capable of inflicting immediate injury or death. Among these agents are a wide variety of drugs, cleaning, polishing and disinfecting compounds plus an array of substances such as lead-based paints, perfumes, lighter fluid, alcohol, turpentine, gasoline, solvents and thinners, pesticides, and other materials. In fact at any one point in time, there are approximately 250,000 chemical products which are capable of causing human illness, death, or contamination to wildlife and the environment. It has been estimated that approximately 40,000 new potentially poisonous products enter the market each year. In less than 20 years, the use of synthetic chemical pesticides has increased from a level of a few million pounds a year to nearly one billion pounds annually. Today, almost 60,000 different pesticide formulations are now registered in the United States and each of these contains one or more of the approximately 600 different pesticide compounds.

Pesticides have had a tremendous impact on the benefits we have been able to derive from our society. If, for example, we are to look at some of our recorded history, we would find that the literature is replete with writings pertaining to man's continual battle to eliminate or reduce populations of pests.

In the early history of the colony of Virginia, Captain John Smith recorded that in 1609:

> In searching our cashed corn, wee found it halfe rotten and the rest so consumed with the many thousand rats increased from the ships, that we knewe not how to keepe that little we had. This did drive us all to our wits ende; for there was nothing in the country but what nature afforded (2).

Later in 1617, he wrote of rats again:

> .....they spared not the fruits of the plants, or trees, nor the very plants themselves, but ate them up.....at last it pleased God, but by what means it is not knowne, to take them away (2).

An arsenical compound, copper acetoarsenite (Paris green) was used as man's first pesticide; discovered in 1867, this chemical was first used to control the Colorado potato beetle. Later pesticides played important roles in stemming outbreaks of yellow fever, malaria, typhus and other vector-borne diseases. While these diseases have been virtually eliminated from the United States, they still remain as threats to the health of people in other areas of the world and pesticides play a vital role in their control.

In addition to the prevention or elimination of disease, pest control measures are necessary to provide the foodstuffs, fiber and other agricultural items necessitated by our expanding population. The total quantity of food eaten each year by the population in the U.S. is sufficient to stagger the imagination. The average sized U.S. family of 4 people consumes over 2-1/2 tons per year. Meat, poultry, and fish account for nearly one-half a ton, and dairy products close to three-quarters of a ton; fruits and vegetables for well over a half a ton; flour and cereal products, sugar, potatoes, fats and oils, and eggs add up to over four-fifths of a ton. Based on these figures, the U.S. consumer averages more than a ton of food per person per year (3).

The food supply of the country must increase in relation to our expanding population. During 1969, the number of farms in the United States dropped to a new low of 2,971,000. This represented a 54.1% decrease from the 6,500,000 farms 50 years ago (4). Associated with the decline in farms is an obvious shrinking of the total number of acres available for agricultural purposes. Obviously, if the nation's food needs are to be met, the productivity per acre must be increased. Pesticides and other agricultural chemicals play a vital role in this connection. In fact it has been estimated that approximately 70% of the most important agricultural crops produced in the U.S. cannot be grown successfully without the use of insecticides. Damage by insects lowers the appearance and general quality of fruits, grains, and vegetables. Almost all corn and sorghum are planted with organic fungicides for the control of decay. Weed control is necessary and carried out by the systematic application of herbicides. More than 50 different species of insects prey upon stored food and grain products. Insecticides play an important role in keeping damage of these commodities to a minimum. Even with the use of pesticides, the loss of agricultural commodities may exceed $11 billion a year (3).

Thus, we are concerned with the widespread dispersal of pesticides and other chemicals in our environment and consequently are placed in a "benefit vs. risk" situation. That is, the advantages to our society must outweigh the detrimental impact the chemicals may have on our environment.

Morbidity and Mortality Associated With Chemicals

During the pre-World War II era the hazards associated with the use of many common chemicals went unheeded; the nations of the world were occupied with more pressing problems. In 1940 a British article implicating aspirin in numerous deaths was published (5). In that year alone, this agent was held accountable for 43 suicides, 8 accidental deaths and 14 unclassified fatalities in Great Britain.

A series of cases involving accidental deaths from acetylsalicylic acid was reported from the United States in 1950 (6). At that time it was revealed that from 1926-1943, a total of 227 persons had died as the result of consumption of excessive amounts of this chemical. These deaths were associated with the increase in productivity of just one of the salicylates--acetylsalicylic acid which had exceed 9,000,000 pounds in one year. Medicants of various sorts have been shown to play an important role in childhood morbidity and mortality. For example, oil of wintergreen was responsible for 6 deaths among children in England from 1931-1939, and 17 from 1940-1949 (7). The same chemical accounted for 28 deaths among children in the United States in 1951, and 34 in

1952 (8). Other products of concern have been broadly classified into disinfectants, antiseptics, household poisons, poisonous plants and a "miscellaneous" category (7). The article by the British investigator (7) prompted a review of the accidental poisoning problem in the United States (9). The basic assumption was that the mortality rate among children in England was the same as that for children in the United States during the period 1940-1950. This was not the case, however, and instead of the expected number of 900 cases in the U. S., there were actually 3,659. Racial differences between the two populations were originally assigned as being responsible for the high number of deaths. While medicants (drugs) accounted for approximately two-thirds of the cases in England, only about one-third of the cases in the United States could be attributed to this source. In the United States in the period between 1949 and 1950, the most common agent was shown to be aspirin and the salicylates which caused a total of 113 deaths in children under 5 years of age. Barbiturates were second in line and accounted for 31 deaths. Iron poisoning, which is common in England is rare in this country, with only two cases being reflected in this review. More than 100 deaths in one year in the less than 5-year-old group were shown to be due to the ingestion of petroleum products. Poisoning from this cause was one of the major factors responsible for increasing the rate in the United States over that in England. In an article published in 1953, a Scottish investigator reported on a detailed investigation of poisoning episodes in that country (10). It was indicated that while only five cases of accidental poisonings were seen at the hospitals in Edinburgh in 1931, by 1951, the number had risen to more than 50 each year. This stimulated an investigation into the accidental poisoning problem in Edinburgh and Aberdeen and the authors reviewed 502 cases that occurred between 1931 and 1950. The agents which were responsible for illness among children in this study population included disinfectants (39 cases), kerosene (31 cases), turpentine (25 cases), bleach (22 cases), barbiturates (36 cases), iron preprations (24 cases), salicylates (20 cases), camphor (29 cases), laburnum (15 cases), and a variety of other materials.

The concern over the problem of accidental poisonings in the United States provided the impetus necessary for the establishment of Poison Control Centers (11), (12). The first center was established in Chicago in the latter part of 1953. This center, which operated on a city-wide basis, combined the efforts of the department of pediatrics of all five medical colleges in Chicago, the Chicago Board of Health, the state toxicological laboratories, the Division of Services for Children of the University of Illinois, and the six major teaching hospitals in Chicago. An advisory committee that included representatives of the American Medical Association, the National Safety Council and the Food and Drug Administration was formed. Each participating hospital was provided with a summary of references to the basic toxic constituents in the thousands of materials in the average household. An outline of the current knowledge of treatment for ingestion of these materials was also made available to each of the participating hospitals. An attending pediatrician was designated as the poison control officer or liaison person to the central committee and was made responsible for making certain that the necessary equipment and supplies were readily available in the emergency rooms, orienting staff members to the problems of poisoning and for filing reports with the Chicago Board of Health. By March of 1958, 124 centers were in operation in 40 different states (11). This was later increased from 356 centers in 41 states to 580 centers in 49 states in 1969 (13). The general purpose of the centers is to minimize the damage from potentially toxic substances by improving and extending efforts for the prevention and treatment of poisoning. The Public Health Service reacted to the chemical poisoning problem in 1957 by the establishment of the National Clearinghouse for Poison Control Centers (12). This group serves the local centers by providing information on new products, by maintaining detailed lists of the ingredients of all household products and drugs. Also, the clearinghouse receives reports of any new poison hazard discovered by any of the local centers and forwards the information to all other centers. The clearinghouse also issues a monthly newsletter, analyzes poison cases and conducts research. The establishment of the Poison Control Centers provided the framework for the conduction of detailed studies of chemical poisonings in many communities throughout the United States.

Among those scientific articles which have been published since the establishment of the Poison Control Center network are several dealing with the epidemiologic analysis of case reports submitted to the National Clearinghouse (14), (15) and others reporting specifically on the chemical poisoning problem in selected metropolitan areas such as Chicago (16), New York (17), (18), (19), Salt Lake (20), and Syracuse (21), (22). One of these reports (10) was on an analysis of 3,926 cases of accidental poisoning. The age group of five and under accounted for 96% of the cases occurring in children under age 15. Males were reported to be involved in 53% of the cases. Medicinal agents (aspirin, barbiturates, non-barbiturate sedatives, tranquilizers) were the offending agents in 2,152 cases (54.8%). Household preparations such as soaps, detergents and bleach accounted for 561 ingestions (14.3%) followed by pesticides (315 cases - 8%) and a variety of other products. A later paper (15) reviewed in detail the results of 15,094 individual case reports submitted to the clearinghouse. A similar pattern of age distribution was shown, with approximately 90% of the cases occurring in children less than five years of age. Internal medicants were ingested in 41% of the accidents and aspirin was reported in over 50% of these cases. Where the type of aspirin was known, the "baby" type accounted for 84% of this total. Household cleaning and polishing agents were ingested in 17% of all the accidents. Ten percent of all the reported ingestions involved pesticides -- the majority of which were due to insecticides. This article differed from those previously published in that an attempt was made to determine the type of container the ingested substances were found in at the time of the accident. In one-third of the total cases, the chemicals were not found in the original container. The room of the house in which poisoning accidents occurred most frequently was the kitchen (40%) followed by the bedroom (22%) and the bathroom (12%). The remaining incidents took place in the basement, living room, garage and other areas. A study in Chicago (16) reported data involving 1,033 cases of poisoning between December of 1953 and May of 1955 at 19 different hospitals. A pattern characteristic of that shown earlier was found. Medicines were the primary agent in that in 523 incidents (50.6%) of all the cases were due to these substances. Aspirin was the agent of choice in 210 cases (20.3%) of those due to medicines. Cleaning, polishing and sanitizing agents figured in 196 cases (19%) with bleach the most frequently ingested chemical in this category. Poisoning involving pesticides took place in 107 cases (10.4%) of the total. Insecticides were the primary agent in this classification followed by rodenticides. The authors indicated there were 6 fatalities in children under 10 years of age which could be classed as accidental, whereas 6 deaths that occurred among persons from 22-48 years of age could have been accidental or suicidal in intent. The agent at the time of ingestion was stored in the kitchen in the majority of cases, followed by the bedroom, bathroom and other locations. A predominance of the cases occurred among persons residing in low socioeconomic areas, but the writers admitted the possible bias in this conclusion was appreciable. Chemical poisonings (excluding those due to gas) are the third leading cause of death in children under six years of age in New York City (17), (18), (19). In 1954, 454 cases of chemical poisoning occurred in children under 16 years of age in that city. Drugs were responsible for 47% of all poisonings with aspirin as the chief offender and barbiturates as the second leading cause in this category. Bleaches were the primary agent in the household preparations class. Thirteen deaths were reported among children as the result of the ingestion of lead-based paints. This finding corroborates similar investigations of lead-paint poisoning episodes in other areas of the United States such as Philadelphia (23), Baltimore (24), St. Louis (25), Cleveland (26), and Chicago (27). A 1955 study reinforced the problem of accidental poisonings in children in New York City (18). Thus, it was pointed out that there were 21 attempted suicides with chemicals reported in children ranging from 11 to 16 years of age. Age 13 was a high risk category and accounted for nine incidents. Eighteen of the cases occurred among females and three among males. Aspirin was responsible for 10 poisonings, followed by barbiturates, iodine, bleach, tranquilizers, antiseptics and other agents. While no fatalities were reported among this group, seven fatal cases were reported in children ranging in age from 10-24 months. A substantial increase in the number of poisoning incidents between 1960 and 1961 prompted the publication of a paper on the subject (19). This increase was attributed to the improved reporting by physicians. Sixty-six fatalities from poisonings occurred during this period with barbiturates as the chief cause. Ten fatalities from barbiturates were reported in the adult group and resulted mainly from suicides. Six fatalities occurred in children under five years of age of which four were due to lead poisoning, one to a talcum powder ingestion and one from cough syrup poisoning. The reported number of cases rose from 5,070 for a six-month period in 1960 to 6,414 for the same time interval in 1961. A study in Salt Lake City, Utah in 1953 and 1954 pointed out there were 479 persons treated for chemical poisoning in those years (20). These cases occurred among children (311) and the remainder (168) among adults. Drugs were by far the most common cause of poisoning in both children and adults. Aspirin accounted for 27% of all the cases in children. Four persons died from the consumption of chemicals, one child from cyanide and three adults from cyanide, strychnine and alcohol. An attempt was made to study the prevalence and characteristics of accidental poisoning in an urban population in Syracuse, New York (21), (22). The authors obtained their data by direct interviews with a 2% sample of the total population of this city. Thus, 1,069 families with 4,069 members were selected and considered to be reasonably representative of the total city population in age, sex and socioeconomic status. A total of 107 poisoning episodes were recorded as having taken place among the study population. Physicians were consulted in only 79 of these cases or 74% of the total. Some of the persons interviewed were not aware of the hazards of aspirin and 36% of the ingestions in this category were not brought to the attention of a physician. This was contrasted with the experience in other types of poisoning where 80% or more of the patients sought medical attention. A total of 53 of the ingestions (58.9%) were due to medicines, with aspirin the chief offender in this class. The remaining ingestions were due to household products, petroleum-based chemicals, pesticides, paint and paint products, cosmetics and other agents. The authors were not able to demonstrate any geographic or socioeconomic aggregation of cases.

A paper published in 1961 reported upon the poisoning morbidity and mortality from England and Wales (28). The data was obtained by selecting a 10% sample of all patients discharged from the National Health Service hospitals (excluding the mental hospitals). From these records, 1,000 consecutive records of poisoning were extracted; 218 of which occurred in children under 15 years of age. Fifty percent of these cases were shown to involve the ingestion of pills, tablets and other medicinal substances. Aspirin was involved in 44 of the cases, followed by barbiturates in 28 cases and other substances in 33. Disinfectants ranged high among the household products group. Berries and plant substances were responsible for 8 cases. The number of fatalities among children poisoned accidentally in England and Wales is about 44 per year. As with the hospital admissions, aspirin and salicylates head the list as the most common causes of death. Iron preparations were responsible for 12 deaths and 10 deaths were attributed to strychnine.

Attention has been focused upon the role of pesticides as causative agents in accidental poisonings (29), (30), (31), (32). The prevalence of injury from pesticides on a nationwide scale is difficult to determine. California is the only state which annually publishes a detailed tabulation of non-fatal injuries from economic poisons (29). The difficulty in compiling reliable pesticide poisoning statistics has been due to the lack of uniformity in identifying and recording agents responsible for injury. For instance, only 17 items in a total of 446 entries listed under the category of poisoning in the International Statistical Classification of Diseases, Injuries and Causes of Death relate to pesticides. There are, however, over 400 basic pesticide chemicals and approximately 60,000 formulations now available. In a study of deaths due to pesticides it was shown that there were 196 deaths reported in 1946, 154 (1947), 157 (1949), 152 (1950), 132 (1952), 133 (1953), 105 (1954) and 140 (1955) (29). Morbidity data submitted by various reporting groups such as industrial commissions and poison control centers support the conclusion that only the more familiar materials used as pesticides are included in this category. A later report (30) included data on mortality from pesticides for the years 1956 to 1960. Pesticides were reported as the cause of death in 141 cases (1956), 111 cases (1958), 130 cases (1959) and 103 (1960). A paper published in 1964 (31) speculated that the rate of deaths from pesticides is now about one per 1,000,000 persons each year. It was further indicated that there has been no change in the death rate associated with the increasing use of the newer pesticides. Detailed investigations conducted in certain areas of the United States do not concur with this finding. For example, in Dade County, Florida, which has a population of 1,040,000, 89 deaths were due to pesticide ingestions from 1956 to 1964. This statistic includes 23 cases designated as accidental, 52 as suicidal and 4 homicides. Parathion, an insecticide not specifically listed in earlier papers, was shown to be responsible for 9 of the 10 deaths among children over a four-year period (32). A unique problem in Dade County is the illegal door-to-door sale of parathion in unmarked containers. This activity in itself has been shown to be responsible for the deaths of several children.

The etiology of accidental poisoning episodes has been the subject of considerable investigation. In addition to those factors indicated earlier with regard to the storage of chemicals in containers not intended for that purpose, and the accessibility to chemicals, other facets of the problem have been explored. For example, the role of oral abnormalities has been presented (33). It was indicated that those children who poison themselves can be divided into two groups. The first of these is composed of those children who take the poison (usually in the form of attractive tablets or liquid) from a bottle, but who taste or chew the substances and in the majority of cases, reject it before harm results. The second group of youngsters show exaggerated oral traits, amounting to pica in about 50% of the cases, and poison themselves with tablets of any kind. Tablets attract them more than liquids and if they have access to candy-flavored tablets such as aspirin or ferrous sulphate, they may ingest them in lethal quantities. The risk of death to children is greater in the latter category than the former. An attempt was made by an Australian writer in 1956 to correlate social factors with accidental poisonings among children (34). Thus, it was pointed out that negligence or carelessness on the part of the parents is an uncommon cause of poisoning. Based upon the results of follow-up investigations the authors indicated that 79% of the mothers of poisoned children were shown to be careful and handle their children well. It was also shown that 63% of the 155 cases originated from "standard" homes and that 79% of the fathers were professional or businessmen, or skilled tradesmen. The smaller number of children originated from poorer families who belonged to the laboring or semi-skilled groups who had a lower material standard of living. Connected with the possible social factors of accident causation have been attempts to explore the relationship associated with persons repeatedly poisoned (35), (36). One of these papers (35) described data which was based upon the study of a group of 100 children who had experienced one episode of accidental poisoning. A group of matched controls were selected from a previous randomized population derived from the city of Syracuse (22). The poisoned group was found to have many more subsequent episodes of poisoning than the control group. These children were more active and mischievous, were more likely to experience falls, and had more frequent separation experiences from their parents. The girls among the repeater group were described as being more boyish in behavior and both sexes walked earlier than those members of the control group. In a later study (36) the families of 20 poison repeaters, 19 single ingestors and 13 controls were studies. It was shown that social class, religious affiliation, income, geographic setting and family size do not seem to be correlated with repeated episodes of poisoning in children. This study refuted earlier work and it was indicated that repetitive poisoning is not related to accident proneness, pica, environmental hazards or lack of parental supervision. The ingestion of poisons seemed to be the result of purposeful behavior on the part of the child. The first ingestion may be the result of the child's negativism, imitation of the parent's pill taking or confusion with food. Subsequent ingestions were described as being the methods the children use to gain more relatedness with their parents or to express anger or negativism. A study published in 1968 (37) presented information that suggested that parental ignorance of toxicity, and carelessness in storage are merely secondary environmental factors which may be manipulated to decrease the ease and frequency with which the accident occurs. A statistically significant relationship was found between "pica" and "daredevilness" in children and poisoning accidents. There was no statistical difference that could be demonstrated with regard to the mother's knowledge of the toxicity of medicines and household products nor in the number and storage pattern of potentially toxic substances accessible to children.

The scientific literature contains a variety of published reports relative to methods and programs for the prevention of accidental poisonings. The most successful of these ventures in terms of reducing mortality among children was the establishment of the Poison Control Center network which was referred to earlier. The influence of these centers on morbidity is difficult to determine since the centers are not located in all urban and rural areas and are operated on a voluntary reporting basis. In any event, numerous suggestions have been presented for reducing the health problems associated with chemical poisonings. Among these are the proposals relating to the labeling of containers containing chemicals (38), (39). The need for the precautionary labeling of chemical products was first formally expressed by the American Medical Association in 1884 with the adoption of a resolution urging that Congress and the state legislatures be called on to enact legislation requiring containers of lye to bear a poison label (39). Specific warning statements are required on various types of products in order to conform to the requirements of the Federal Food, Drug, and Cosmetic Act, the Caustic Poison Act and the Federal Insecticide, Fungicide and Rodenticide Act (29). The influence of these statements on morbidity and mortality among children is difficult to assess since most children in the five and under age group are not capable of reading. An attempt has been made to determine the degree of "attractiveness" of certain medicants, particularly aspirin, to children (40). The results of a study indicated that bright colored tablets were the most popular among children with magenta ranking first. Brown, a dull color placed high among the study population, presumably because of its similarity to chocolate. Wine and black-colored tablets were found at the lower end of the list. Thus, the author proposed that aspirin and other drugs be incorporated in black-colored tablets and that the tablets be dispensed in plastic strips which are difficult for children to tear. The use of safety closure caps on drug containers has been proposed (41). The author investigated 14 different types of safety caps over a period of three years. Two caps were finally selected for comparison with the conventional screw cap in a test area of 1,600 homes that had children under five years of age. The two experimental caps were found to be difficult to remove by over 93% of the children in the survey. The author concluded that a safety-type cap is practical and a good safety measure of real importance. A later study (42) showed that poisonings among children can actually be reduced by the use of bottle closure devices. In a study in the Tacoma, Washington area, the author indicated that the rate of accidental poisonings from tablets dropped from one per 5,100 prescriptions to one per 62,300 prescriptions. Poisonings due to "children's" flavored aspirin were reduced by 97%. Similar results were reported from a Canadian investigation (43). Two scientists have attempted to study the accidental poisoning problem among children by ascribing the preventability of the episode (44). The authors found three circumstances which occurred singly or in combination that accounted for 86 of the 100 poisonings investigated. In 26 cases, some person other than the parents (siblings, other children, neighbors, relatives, friends) played an important part in the episode. These individuals may have made it possible for the poisoned child to reach the substance, or they may have failed to properly store the chemical. In 31 cases, the parents did not think that the child could climb, open doors, unscrew caps or perform other tasks necessary to obtain the agent. In 53 cases the poison was not in its usual location, either because it was in use, because persons other than the parents had left it out or because the parents themselves were careless. Many accidents could be avoided by parents abstaining from taking medicines in front of their children (45). A detailed study in the Norwalk, Connecticut area corroborated the findings that children will imitate their parents by ingesting chemical substances. It was shown that of the children poisoned by medication other than aspirin, 67% frequently observed their parents taking pills. This was found in only 13% of a comparison group who ingested "baby" aspirin. The author indicated that this factor is suggested as playing an additional role in causation and could be minimized by proper parent education (46). The traditional approaches to public health education have also been suggested as beneficial to the reduction of accidents from chemicals (47). Included among the educational techniques which have been employed are films, exhibits, lectures, demonstrations and the establishment of poison prevention programs with community health councils, Parent-Teacher Associations, 4-H clubs and similar organizations. A study conducted in Charleston, South Carolina in 1962 and 1965 (48) demonstrated the feasibility of a concentrated, community-wide program to reduce the incidence and severity of accidental poisonings. This survey pointed out that lack of awareness on the part of adults still exists at all socioeconomic levels. One of the newest approaches to poison prevention has been the establishment of Poison Central (49). This arrangement, which was established in Kentucky in 1962, provides a master toxicology information and service facility for the state's system of regional poison information and treatment centers. Poison Central operates on a 7-day-a-week, 24-hour-a-day basis and provides toxicologic services not available at regional centers or at local hospitals and clinics. Additionally, the unit provides readily accessible services for areas not served by poison control centers.

The deliberate ingestion of chemical agents or the so-called "therapeutic misadventures" or self-poisoning episodes, with or without suicidal intent, are a problem of great concern. Attention to this problem, particularly among young individuals was noted in New York City after the establishment of the Poison Control Center in 1955 (50). The author of a paper on this subject in the New York area indicated that 299 suicidal attempts by poisoning were reported in individuals less than 20 years of age. These episodes took place between March of 1955 and December of 1958. Females accounted for 232 cases or 78% of the total, whereas males were accountable for 67 cases. Puerto Ricans, who compose 11.8% of New York

City's population were responsible for 28% of the attempted suicides. The primary agents involved were aspirin (84 cases--28%), barbiturates (47 cases--16%) and tranquilizers (36 cases--12%); the remaining cases were attributed to bleach, iodine, lye, insecticides and other chemicals. A definite seasonal pattern was pointed out with the incidence lowest in the autumn and highest in the spring. The type of agents employed in the New York City cases have been implicated in similar episodes elsewhere (51). One writer (52) speculated upon some of the predisposing causes to suicide. In his report, he discussed two cases involving the ingestion of chemicals. One of these involved a 14-year-old male who swallowed an unidentified toxic agent to prove that he was invulnerable. Another concerned a 12-year-old girl who attempted suicide by taking a large amount of sedatives because she dreamed of her dead mother and wanted to join her. The hazards to health as the result of the availability of proprietary drugs like scopolamine have been questioned, because of the involvement of these chemicals in self-poisoning incidents (52). This chemical has been the subject of many reports, including one from Casper, Wyoming (52). Six cases involving suicidal ingestions were treated in that community over a six-month period. The authors of a paper on the subject takes exception to those advertisements that emphasize the "safe" or "harmless" character of sedatives containing this chemical. In another paper (53), the investigators reenforced the views of those presented in previous articles with reference to this agent. The toxic dose is reported to be about 3-5 mg. (12-20 tablets). The authors indicated that from their experience, self-induced drug intoxications usually involve five main classes of agents. Among these are the barbiturates, salicylates, glutethimide, meprobamate and phenothiazines. Their experience also indicated that ethylene glycol, bromides and scopolamine preparations are frequently ingested with suicidal intent. A study dealing with the various aspects of self-poisoning in the Chicago-Cook County area has been published (54). In 1964, 468 persons were treated for deliberate poisonings in the adult emergency department at Cook County Hospital. The preponderance of persons in the group were females (333 - 73%) as compared to 135 males. Persons less than 45 years of age made up 84% of the group. More than half of these were less than 25 and a large number were teenagers. The patients ingested 102 different drugs and chemicals. Barbiturates were again the agent of choice, followed by the salicylates and tranquilizers. Rubbing alcohol, bleach, antiseptics, and rodenticides were also used as self-destructive agents. Two comprehensive studies on self-poisoning episodes have been issued by the British in recent years (55), (56). For example, in the Oxford area, it was shown that 502 females and 200 males were admitted for treatment of self-induced poisonings between 1962 and 1965. The patients ranged in age from 11 to 85 years. Females outnumbered males in all age groups. The authors reported that there were forty double admissions, seven triple, two quadruple and one sextuple. The main poisons used were barbiturates (45% of the cases) and aspirin (26%). The frequency of the usage of barbiturates rose steadily with age from 23% of the admissions under the age of 20 to 60% in persons age 50 and older. Over the same age span, the use of aspirin declined from 49 to 12%. The highest rate of self-poisonings was observed among married females under the age of 20. Unmarried girls in the same age bracket had a different rate which was of statistical significance. Married women showed slightly higher rates than single women at all other ages, but both groups showed diminishing rates above the age of 25. Of the total number of persons in the study population, 8 deaths were recorded (55). In the Cardiff, Wales area, all cases of intentional poisoning that were admitted for treatment between the years 1950 and 1965 were studied (56). During the period indicated, a total of 1,736 deliberate poisoning episodes were recorded. A total of 300 of these events occurred in females less than 25 years of age. But, the preponderance of cases (436) occurred in females between 25 and 45 years of age. The same pattern was true for males in that 199 individuals were reported to have been in this age bracket. Attempts were made to associate significant organic illnesses with the poisoning gesture. It was demonstrated that 20% of the individuals did have some illness at the time of the episode. Twenty-six percent of the patients had been under psychiatric care and a further 38% were known to have been suffering a mental illness of one kind or another before the episode--mainly depression. The agents used in these incidents were barbiturates, salicylates and coal gas (carbon monoxide) which together accounted for 70% of the attempts. The number of fatalities that resulted from the ingestion of these and other agents was not specified. The preference of barbiturates over other methods of committing suicide has been pointed out (57). This was done in a report of the suicide problem in two cities, namely, Los Angeles and Vienna. In one recent year, barbiturates and other drugs and chemicals were responsible for 30 deaths in the former city and 31 in the latter. The employment of chemicals was second only to domestic gas and hanging in Vienna and shooting in Los Angeles. The difficulty of trying to learn of the prevalence of suicidal attempts in a community has been reported (58). Thus, it was pointed out that 45% of the attempts involved narcotics, 15% salicylates and 20% were due to other chemical agents. The remaining attempts were due to hanging, slashing of the wrists and other means.

The prevention of deliberate poisonings involves the application of numerous techniques. Among these are the proper counseling of persons with psychological problems and the maintenance of proper controls over drug items. Persons ill from an overdose of a toxic chemical must receive a proper diagnosis and treatment, and surveillance should be maintained over persons in high-risk categories.

Heavy Metals

During the past few years, there has been considerable publicity in both the lay and scientific press with regard to three heavy metals--mercury, lead, and arsenic. Each of these agents creates special problems in our environment and will be discussed separately.

Mercury

The hazards associated with mercurial compounds have been known since ancient times. Inorganic mercurials were used as suicidal agents, abortants, and for therapeutic purposes for many years. Mercurialism as a result of industrial exposure has been a problem of concern for quite some time. The expression "mad as a hatter" exemplified the presence of the illness in the felt hat industry. "Minamata disease" or methylmercury poisoning due to the ingestion of contaminated fish, occurred in a village near the Minamata Bay, Japan, from 1953 through the 1960s. The condition affected at least 121 children and adults of whom 46 died. Attention was again focused on the disease in 1964 and 1965 in Niigata, Japan when 47 persons became ill, 6 of whom died (59). These episodes, and an incident in Alamogordo, New Mexico involving a family of 7 in 1969 served to focus attention on the hazards associated with the presence of this agent in the environment.

Mercurial compounds may enter the biosphere from any number of sources. Paper pulp factories which use mercurials to prevent the growth of slime from fungi frequently discharge PMA (phenylmercuric acetate) with their waste water. Paper products which retain mercury and are subsequently combusted might contribute to atmospheric contamination. Industrial concerns which use mercury electrodes in the production of chlorine and caustic soda often release mercury into the air and water. Laboratories where mercury is used in devices for analyzing blood specimens and central supply rooms in hospitals where mercury is frequently used to clean scientific instruments can be a source of concern. The runoff from agricultural areas which have been treated with mercury-based pesticides are a frequent source of contamination to the aquatic environment. Fungi-resistant paints containing mercurial compounds may be a source of contamination to the persons applying them and subsequently to others that may be exposed to the painted surfaces. Mercurials are often used as mold suppressants by commercial laundries, particularly those with diaper services.

The fact that all forms of mercury entering the aquatic environment may be converted to methyl mercury, which is more toxic than other forms, and can be concentrated by fish and other aquatic species is a problem of growing concern. Alkyl mercurials can be introduced into the food chain by the consumption of mercury-treated seeds or meat from animals which have been fed these compounds.

We must be continually aware of the health implications from mercurials and must conduct appropriate procedures to monitor their dissemination in the environment.

Lead

Despite modern scientific advances, lead poisoning or plumbism remains a unique public health problem. The incidence of chronic lead poisoning in children is greater today than in adults, and the fatality and disabling effects are much more marked in children. Occupational poisonings in adults as a result of inhalation of the dusts and fumes of inorganic lead are still of concern.

The environment is subjected to contamination by the leaching of lead from geologic formations. It has been estimated that man's activity in the United States alone in 1966 added approximately 700,000 tons of lead to the environment in that year. The contribution of lead from tetraethyl lead in motor vehicle exhausts has been estimated to be 185,250 tons (60). Contamination of the soil and vegetation from air pollution is related to traffic volume. Only a small part of the lead released from vehicle emissions settles and accumulates in the vicinity of the roadways. The majority of the material is transported by air currents and ultimately settles on the soil and vegetation. Lead which has been recovered from surface waters has been attributed to gasoline. This may result in the accumulation of lead in the tissues of fish.

Lead poisoning among children has been the subject of considerable investigation in Philadelphia, Chicago, Baltimore, Cleveland and many other urban areas in the United States. The study in Cleveland confirmed that the susceptible host for lead poisoning is predominantly a pre-school child with a history of pica and that the agent is found in an environment which is easily definable. Continuing investigations of children residing in tenement dwellings, the development of improved analytical techniques and environmental measures are necessary in order to keep lead poisoning cases among the younger population to a minimum.

Arsenic

Throughout history, arsenic has acquired unequalled notoriety as a poison. As early as 2000 B.C., arsenic trioxide is reported to have been obtained from smelting copper and subsequently was used as both a poison and for medicinal purposes (61). The word "arsenic" appears to have been derived from the Greek word "arsenikon" meaning "potent" (62). An arsenical, copper acetoarsenite (Paris green), was also used as man's first pesticide; discovered in 1867, this compound was first used to control the Colorado potato beetle.

The use of arsenicals as insecticides is declining in the United States. On the other hand, the use of the arsenical sodium arsenite as a herbicide has increased because of the shortage of certain chemicals (2-4-D and 2-4-5-T in particular) brought about by the Vietnam war. In other parts of the world, the use of arsenicals (as herbicides and insecticides) has apparently not declined or increased significantly in recent years (63). The use of arsenic as a rodenticide has declined in the United States as a result of the advent of the anticoagulant rodenticides.

One publication (64) lists 55 different situations and/or industrial processes within which arsenicals are utilized in one form or another. For example, they are used as decolorizers of glass, pelt preservatives, grasshopper bait, larvacides, amebicides, additives to animal feeds, algicides, and a host of other applications. This same publication points out more than 100 different population groups that may have occupational and/or environmental exposure to arsenic. The list includes airplane pilots, farmers, pest control operators, taxidermists, tannery workers, and many other individuals.

Lead arsenate has been used extensively in the past for the control of insects associated with apple orchards, vineyards, and tobacco crops. It is still used to a limited extent for the control of the Japanese beetle and the boll weevil. Arsenic trioxide is used mainly as a long-term soil sterilant. Sodium arsenate is frequently used as a nonselective spray to control all types of vegetation; however, since this compound has a salty taste, its use in areas frequented by cattle is to be discouraged. Sodium arsenate is also used for aquatic weed control and as a soil sterilant. Disodium methyl sodium arsonate (DSMA) is less toxic to humans and pets and is used for the control of Dallas grass in lawns and turf. Calcium arsonate is used as a preemergence herbicide for the control of crabgrass and chickweed in lawns and turf (65). In recent years the unique herbicidal properties of cacodylic acid and of methyl arsenic acid were discovered. These simple acids, among the first organic compounds known, are highly toxic to plants, but relatively nontoxic to man and animals. The U.S. Forest Service has developed a hatchet that automatically injects cacodylic acid when a blow is rendered to a tree--thus a new application for this material as a silvicide has been created. Arsenic acid is used as a defoliant to facilitate mechanized harvesting of cotton. As postemergence herbicides, the use of simple arsenicals is unsurpassed. They leave token residues and permit germination of the new seed promptly after the undesirable plants have been destroyed (61).

Thus, with this brief background, it can be readily seen that a significant proportion of the population, if not all, is or has been exposed to an arsenical by one means or another.

Man comes in contact with the arsenicals in a variety of different ways. The degree of exposure may be related to a person's occupation, the proximity to a copper smelter, the nature of foods consumed, the type of soil in the areas, the type of arsenical ingested or applied for medicinal purposes, and a multitude of other factors. For example, shellfish have been shown to contain high amounts of arsenic when harvested from waters containing 0.14 to 1.0 PPM of this chemical (66). Fish are known to concentrate arsenic in their tissues. Residues as high as 40 PPM have been obtained from the oils and tissues of black bass taken from waters in the southern United States. No arsenic was found in a specialized study of the public water supplies of the 100 largest cities of the United States. The maximum allowable concentration of arsenic for potable waters in various countries ranges from 50 - 150 PPB. The usual daily intake from water in the United States is estimated between 10 and 20 μg. (63). The detection of arsenic in varying amounts in different foodstuffs has led to the establishment of tolerances for this chemical. At the present time, tolerances for arsenic on foodstuffs range from zero in the Soviet Union to 4 PPM for arsenic acid in raw cottonseed meal, 2.6 PPM on most foods, and 50 PPB in water in the United States.

Food products can become contaminated with arsenic in many ways. For example, apples that have been sprayed with lead arsenate for codling moth control can contain as much as 1 to 2 mg. of residue. Wine and cider can contain arsenic, but this is usually removed during processing. Wine yeasts have been shown to contain arsenic in amounts up to 150 - 180 PPM and baker's yeast up to 17 PPM. Meat may contain traces of arsanilic acid that has been used as a growth additive in cattle and poultry feeds. Theoretically, these additives are discontinued several days prior to marketing and in fact, the Food and Drug Administration allows a maximal animal tissue arsenic content of 2.65 μg./g. The arsenicals must be removed from the feed 5 days before slaughter so that the total level of arsenic in edible byproducts is below 1 PPM. At permissible feeding levels of these drugs, the arsenic in muscle rarely exceeds 0.5 PPM even without the 5-day withdrawal period.

Soil concentrations of arsenic can rise to several hundred parts per million after years of spraying with lead arsenate and other pesticides. It has been postulated that arsenic tends to remain in the top layers of the soil thus rendering it sterile to the growth of some plants. Small amounts of arsenic may be translocated by plants grown on heavily contaminated soils. The quantities of arsenic which have been obtained from plants grown under these conditions are not considered detrimental to human health. Potatoes have been shown to contain 1 PPM of arsenic whether they were treated with arsenical pesticides or not (67). While other organic pesticides are gradually replacing arsenical sprays on food crops in the United States, the use of arsenic-containing herbicides and defoiliants has increased as indicated earlier.

The arsenic concentration of atmospheric dust has been determined by a number of workers and is reported to be low or absent in most areas. Arsenic has been recovered from the air of areas where coal is burned or smelting operations are in progress. The recommended limit of arsenic in the air is 0.5 mg./m^3. Only minute traces of arsenic have been recovered from the air in the United States. In a survey of 8 English communities in 1952, the arsenic content of air was found to be in the range of 0.037 µg./m^3 (As_2O_3) to 0.075 µg. (64).

Recently, concern has been expressed over the arsenic content of phosphate ores. Phosphates are an essential constituent of many detergents. Thus, many individuals expressed the fact that these compounds may serve to further pollute our aquatic environment. As a result, the soap and detergent industry has directed their research efforts toward finding suitable substitutes for the phosphates.

If we are going to evaluate the impact of these and other chemicals on human health, there are a number of avenues we must explore:

1. We must continue conducting long term prospective epidemiologic studies to determine the significance of low doses of chemical agents on human health. These studies should include investigations of various combinations of chemical agents; e.g., alcohol and carbon monoxide, pesticides and barbiturates.

2. Efforts must be directed toward the development of competency with regard to pesticides and other chemicals by State and local health departments. These chemicals should receive the same emphasis that is currently being placed on communicable diseases. Concurrent with program development there should be a modification in philosophy, that is, that morbidity and mortality from chemical agents like that from communicable disease is preventable.

3. Morbidity and mortality regulations within individual states need to be strengthened by adding the requirement that illnesses and deaths associated with chemical agents be reported to the agency responsible for the collection of vital statistics. This is imperative if we are to logically assess the hazards associated with the use of chemicals.

4. Research must be continued into non-chemical methods of pest control. Concurrent with this, emphasis must be placed upon improved crop rotation practices, the development of insect resistant crops and similar activities which will eliminate or reduce the need for pesticidal chemicals.

5. We must continue to monitor the presence of chemicals in the diet, in the atmosphere, and in our air, water and soil. Data collected from these monitoring activities must be analyzed to determine their relationship to human health.

On December 2, 1970, President Nixon established the Environmental Protection Agency. This unit establishes at the Federal level a strong focal point for environmental health activities. In a recent speech, The Administrator of the Agency said:

"Our goal must be to obtain the capacity to foresee and respond to emerging problems so that the future will not overwhelm us. Environmental problems are hitting us from every conceivable direction. Every time we look at a newspaper we are reminded how ignorant we were yesterday or last year. Asbestos one week, phosphates the next, mercury the week after--and we may be sure others will follow.

"We have been sitting on the sidelines expecting technology to bring us an unmixed blessing of progress and prosperity. We set technology in motion, and expected it to take care of us. In truth, technology was a substitute for thought." (68).

Thus, as is pointed out, it becomes obvious our thinking must change if we are to keep pace with our environmental problems.

Our goal for the future might well be found in the writings of Louis Pasteur who indicated:

"Two opposing forces seem to be in mortal combat today. One, a force of blood and death--ever devising new means of destruction.....

"The other, a force of peace, work, and health, ever evolving new methods of delivering man from the scourges that beset him."

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Introduction to Principles of Toxicology

Thomas B. Gaines

1. Definition: Toxicology is a science that deals with the action of poisonous materials on living cells and tissues, the response of the living structures, and the detection and identification and evaluation of safety of these poisonous materials.

2. Divisions of Toxicology, by Loomis:

Environmental	Economic	Forensic
Pollution	Development of Drugs	Diagnosis
Residues	Food additives	Therapy
Industrial Hygiene	Pesticides	Medicolegal Aspects

3. Scientific Disciplines involved: Chemistry, biochemistry, pathology, biology, pharmacology, physiology.

4. Historical:

   A) M.J.B. Orfila (University of Paris) - Traite des poisons, etc. (1814-1815): Considered by some to be the creator of modern toxicology, he was the first to point to the necessity of chemical analysis for the proof of lethal intoxications.

   B) Henry Coley - American, author of Poisons and Asphyxia (1832).

5. Laws in United States Dealing with Poisonous Substances:

   A) Federal Insecticide, Fungicide and Rodenticide Act- labeling regulations.
   B) The Food Drug and Cosmetics Act - Establishes tolerances to be policed by chemical analysis. Miller Amendment of this Act refers to pesticides applied to raw agricultural produce.

      Food additives Amendment covers materials added to food after harvest.

      Hazardous Substances Amendment.

      New Drugs Amendment.

   C) State laws.

6. Kinds of Injury Which Poisons May Cause:

   A) Toxicity causing death, sublethal symptoms, change in growth rate, photosensitization, etc.

   B) Pathology - organ weight change, gross and microscopic pathology.

C) Hematology and Clinical Chemistry

D) Neurotoxicity - development of paralysis.

E) Teratogenesis - effect on fetal development.

F) Carcinogenesis - development of malignant tumors

G) Hypersensitivity

H) Induction or stimulation of enzymes such as microsomal enzymes of liver.

I) Mutabenesis - genetic change.

J) Changes in behavior.

7. Factors Influencing Degree of Injury:

Compound
Dosage levels
Schedule of dosage
Duration of dosage
Route of exposure
Species and strain differences
Sex
Age
Interaction of Compounds
Nutrition
Disease
Temperature and other environmental factors

8. Chemical Metabolism of Compounds:

A) Biotransformation - conversion to metabolites

B) Quantitative Aspects:

Absorption
Distribution
Storage and storage loss
Excretion

C) Methods of studying:

Tracers
Chromatography
Mass Spectrometry
Metabolic pool technique

9. Selective Toxicity:

The injury of one kind of living matter without harming some other kind with which the first is in intimate contact. The living matter to be injured may be referred to as the uneconomic species, and the matter which is to be unaltered as the economic species.

10. **Tests in Laboratory Animals:**

A) **Route of exposure:**

(1) Oral
(2) Percutaneous
(3) Inhalation
(4) Parenteral by injection

B) **Duration of exposure:**

(1) Acute toxicity - single dose, range of dosage levels given to arrive at LD_{50} value, lowest lethal dose, and lowest dose producing signs of poisoning.

(2) Subacute toxicity - generally considered 90 day test and if by oral route chemical is usually given as a component of the diet.

(3) Chronic toxicity - 2 years in rats and mice, possibly longer exposure in dogs and primates.

C) **Tests to detect teratogenesis and effect on reproduction:**

(1) Teratogenesis - pregnant female dosed during organogenesis to determine effect on fetus.

(2) Reproduction - Animal usually fed chemical in diet at graded levels and studied through 3 generations.

D) **Potentiation** - effect of combination of 2 chemicals in which the effect is greater than additive, for example: 1/4 LD_{50} of one compound plus 1/4 LD_{50} dose of other compound = 1 LD_{50}.

E) **Sensitization**: Injection followed by delay. Then challenge injection given resulting in substantially greater reaction than after original injection.

F) **Eye Irritation:** Chemical instilled in eye and observations made on effect on conjunctive (swelling), cornea (ulceration or opacity), and iris (inflammation).

11. **Factors Affecting Absorption and Toxicity:**

A) **Oral route**:

(1) Type of solvent or suspension agent
(2) Purity of compound
(3) Fasting state of animal

B) **Dermal or percutaneous route**:

(1) Solvent or physical state of material
(2) Area of application
(3) Condition of skin - abrasion of skin increases absorption.

C) Inhalation:

(1) Physical state - dust or aerosols
(2) Particle size: Particles in excess of 20μ in diameter are seldon inhaled. Upper respiratory tract tends to capture particles between 5 and 10μ size, and alveoli are most efficient in capturing particles of 0.1 to μ in diameter.

12. Measurement of Toxicity:

A) 1-dose ED_{50} or LD_{50} - calculated dose to produce some specific effect or death of 50% of test animals.

B) 90-dose ED_{50} or LD_{50}

C) Chronicity factor: 1-dose LD_{50} (mg/kg) ÷ 90-dose LD_{50} (mg/kg/day).

D) Subacute index

E) ET_{50} and LT_{50}: time required to effect or kill 50% of test animals.

F) EC_{50} and LC_{50} - concentration required to effect or kill 50% of test animals.

G) Response to graded dosage levels

H) No significant effect level - Dosage level at which no effect is observed in experimental animals. In reality it may be an indication of our lack of ability to detect an effect. Any amount of chemical that is taken into the body probably produces some effect.

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STRUCTURE-RELATED CHEMICAL CHARACTERISTICS OF PESTICIDES

L. A. Richardson

In the area of chemical properties of pesticides, the only factor more important than chemical structure, is the elemental makeup of the compound. Chemical structure exerts a major influence on the toxicity, reactivity, metabolism and degradation potentials, persistence, and the analytical methodology useful in the elucidating and measuring of most pesticide chemicals. Thus, a basic knowledge of the structural characteristics of pesticides is absolutely essential to all personnel responsible for any area of pesticide use, control, or analysis.

In the short period of time which we have to discuss pesticide chemistry, one can only present an introduction to the fascinating and complex subject. I will, however, provide a brief picture of how these compounds exist in space and how related chemical species differ among the "use groups; insecticides, herbicides, and fungicides. Secondly, I will discuss with you examples of reaction, metabolism, and degradation of type compounds.

First, in order to impress upon you the complexities and importance of pesticide chemistry, please note that there are at the present time some 900 chemical species, from which about 90,000 formulations are available for use. While the problems in pesticide chemistry are not particularly peculiar, the discussion of such a large segment of the chemical industry and the understanding of such a discussion is indeed difficult. In actuality, there are only about 100 chemical species in primary use, about 20 of which we will consider today. Chemical pesticides are produced at about two billion pounds per year at the present time. This is about 10 pounds per capita, or enough poison to kill every human being on the face of the earth. Fortunately, most of these materials are not persistent as the parent compound; and although their decomposition or metabolism may sometimes produce materials which are even more toxic than the parent, generally speaking, the decomposition or metabolism produces compounds which are not nearly as toxic as the parent compound and in some cases are virtually innocuous.

The structural formulae we will inspect are only for the sake of explanation and discussion; there is no attempt here to coerce you into memorizing them since one of your references has each of them cataloged for you. It would be well for you to note and recall important structural characteristics and elemental differences among the chemical species. As a first principle of segregation, we will consider these compounds, one "use" group at a time, beginning with the insecticides.

The chemical species of first importance in the insecticides is the organochlorines. Organochlorines are the most prominent of insecticides because they are the oldest, the most used, and because their toxicity is a two-edged sword. They are relatively non-toxic as far as acute symptoms are concerned, but they are of interest because they are cumulative and may exhibit a more sinister or potential effect. We may also have either a synergistic or an antagonistic activity within the organochlorines themselves or between these materials and other chemical species. In the organochlorines, we have a number of structurally related groups; first of which is the chlorobenzilate or DDT group. The structural relationship depends upon the matrix groups; in this case, we are considering an aliphatic group surrounded by aromatic rings. While virtually each pesticide has both a common and a chemical name, we will consider these materials by their common name; and I will show you how one might arrive at their chemical names. In the chlorobenzilates, we have an aliphatic group as a matrix and the compounds are chemically named on the basis of this aliphatic group. If we look at p,p'-DDT, we find that the matrix is an ethane group. Consequently, the final portion of the chemical name of this compound would be ethane. Tied to the number two carbon of the ethane group are two phenyl groups. On the number two carbon of the ethane group, one finds three chlorines, and in the para-position of the phenyl groups we find a chlorine on each of these aromatic rings. Consequently, the chemical name for this compound would be 1,1,1-trichloro-2,bis-parachlorophenyl ethane. The bis simply indicates that there are two phenyl groups tied to the number two position.

If we look at o,p'-DDT, we find once again that the basic structure, the matrix, is an ethane and again we have two phenyl groups tied to the number two carbon. Once again, we also find that each of the phenyl groups have a chlorine. In this case, however, the chlorine atom of the first phenyl group is in the ortho position. In the second phenyl group, or the prime phenyl group, the chlorine is in the para position as we found in p,p'-DDT. O,p'-DDT, then, is an isomer of p,p'-DDT, a positional isomer. Isomerism changes the characteristic of compounds. In this case, p,p'-DDT is somewhat more toxic than is o,p'-DDT. We also find that we can separate these materials on a gas chromatographic column. That is, they will reach the detector in different periods of time. Methoxychlor has the same basic or matrix group, but the groups associated with the aromatic rings have been changed. We have simply replaced the two chlorines on p,p'-DDT with methoxy groups. We have, of course, changed the toxicity and the characteristics of the compound. Methoxychlor and p,p'-DDT are quite different from the standpoint of toxicity and certain other characteristics. TDE or DDD is another member of this group. In this case, we have only two chlorines on the number one position of the basic matrix while the reactive groups on the aromatic rings are exactly the same as in DDT. The relationship between perthane and TDE is very similar to the relationship between methoxychlor and DDT. In this case, we have replaced the two chlorines on the aromatic ring of TDE with two ethyl groups. Once again, the characteristics of this compound has changed. Kelthane is quite similar to p,p'-DDT. If you look closely, you can see that there is only one difference between Kelthane and DDT and that is that kelthane has a hydroxyl group on the number two carbon whereas DDT has a hydrogen. The characteristics of this compound are obviously different from those of DDT and, as a matter of fact, the chemical name of the matrix group is different. This compound actually has ethanol rather than ethane as its matrix group. If we consider the matrix group to be ethanol, we would also be forced to change the order of numbering the carbons in the molecule. In this case, we would have a 1,1-bis parachlorophenol 2,2,2, trichloro-ethanol.

The second principal group of organochlorine insecticides is the cyclodiene type, or as is sometimes referred to as the aldrin type. These compounds are named on the basis of the cyclodiene group. The three compounds shown in this first group have napthalene as the matrix. As we will note later, when we start talking about reactions, aldrin has a tendency to metabolize or react to form the compound dieldrin. If you will notice, there is a position on the aldrin molecule on which we can institute a minor change and obtain the structure just below, dieldrin. The simple change between these two molecules is a result of oxidation, or as it is usually called, epoxidation. The double bond between the 6 and 7 position of aldrin, which is occupied by hydrogens, has been broken with the addition of an oxygen bridge. Dieldrin is the form in which you normally find the residue of aldrin applications. A compound similar to aldrin which is referred to as isodrin, and to the best of my knowledge is not used as a pesticide, also epoxidizes to the third structure endrin. Aldrin and isodrin are isomers. Similarly, dieldrin and endrin are isomers. These stereoisomers differ in their structure only in that, if we would assume that the solid lines in the chair configurations are in the plane of the screen, the epoxide group in dieldrin would point back into the screen whereas the epoxide group in endrin would point out toward the audience. Once again the properties of the two isomers are somewhat different. Endrin is considerably more toxic than dieldrin. Dieldrin has a greater tendency to concentrate in human tissue, thus I suppose we could say it is more soluble in fatty material. Finally, these two isomers are easily separated on the chromatographic column and emerge and thus strike the detector at different retention times.

The second subdivision of the cyclodiene, or aldrin group, consists of the indene molecules of chlordane, heptachlor, and heptachlor epoxide. Since the matrix of these compounds is the indene ring, they are named chemically as substitutedly indenes. Chlordane is the oldest of this group and unfortunately is still being used to a considerable extent although its usage has decreased in favor of other insecticide agents; one of them being heptachlor. I say that "unfortunately" chlordane is still being used because of two reasons; first, it is the most persistent chlorinated insecticide, and second, it is extremely difficult to analyze by gas chromatography because chlordane consists of a number of isomers and these isomers are separated into a multitude of peaks on the gas chromatograph column. Separate isomers show separate peaks on the chromatogram when using gas chromatography and also give separate spots to some extent (usually a streak) on thin-layer chromatograms. Consequently, they have a tendency to mask other insecticides which might be present and, in addition, cause some difficulty in identifying chlordane itself. Heptachlor is very similar to chlordane and is a popular insecticide although somewhat less popular than it was a few years ago. Heptachlor is never found in human or animal tissues and is found in a rather reduced quantity in any residue determination if one considers the amount applied. The reason for this is that heptachlor readily oxidizes to heptachlor epoxide. This epoxidation is identical to that of the epoxidation of aldrin to dieldrin in that a double bond is fractured and replaced by an oxygen bridge. The resulting product is toxicologically opposed to that of the DDT-DDE conversion. DDE is essentially non-toxic. Heptachlor epoxide, however, is just as toxic if not more so than the parent compound, heptachlor.

The third group of chlorinated insecticides consists essentially of a single compound or, at any rate, a single compound represented by a number of isomers. This is the benzene hexachloride series. I have no hopes of changing anyone's thinking or speaking as we refer to this group of isomers; however, I would like to point out here that benzene hexachloride is a misnomer. This compound, or series of compounds, is derived from cyclohexane. This ring structure is not the benzene ring. It is a cyclohexane and should be referred to as hexachlorocyclohexane. Nonetheless, it has been referred to as benzene hexachloride for so long, just as the organochlorine insecticides have been referred to as chlorinated hydrocarbons for so long, that I'm sure that we will never be able to change the terminology. In addition, I am not entirely sure that it makes a great deal of difference except that for those who are working with these compounds, it is absolutely imperative that we know the correct terminology. The compound pictured is that of lindane, which is the gamma isomer of BHC, the only isomer that is insecticidely active. These are cis-trans isomers and one can readily picture the various transpositions of chlorine and hydrogen in the structure which produce the different isomers. As I indicated, gamma BHC (or HCH as it is sometimes correctly named), or lindane, is the only insecticidely active isomer; however, the beta isomer is a good indicator because it is the most persistent.

The fourth and final group of chlorinated insecticides consists of the fumigate group, some of which are shown. Fumigants are aliphatic compounds and, of course, carry aliphatic names. Methyl bromide, ethylene dibromide, and methylene dichloride are the most popular fumigants. Methyl bromide is a potentially dangerous material whose formulations have been utilized as seed treatment and in the protection of grain in storage. It is applied as a vapor and presents some residue problems in that hydroxyl, sulfhydryl, and amino groups are metholated, and hydrobromic acid is released. Thus, we have an inorganic bromine residue in the product. This pesticide also presents some hazards to the applicator since it is a vapor. Those who apply methyl bromide must take precautions to prevent inhalation.

In spite of the relatively low toxicity of most chlorinated insecticides, they do deserve considerable attention because of the fact that they accumulate in human tissue, particularly adipose, or fatty tissue, and thus may be potentially hazardous. In addition, all of them decompose eventually, but we don't always know the decomposition or reaction products nor the decay rate. We know that chlordane is the most persistent of the chlorinated insecticides and we know that certain others, for example DDT, do decompose or metabolize to a compound which is not hazardous. We also know that all chlorinated insecticides, and for that matter pesticides or reaction products, are persistent in the environment. In spite of the fact that they be removed from our supply by soil binding, leaching, run-off, dilution, plant uptake, or the fact that they are decomposed or metabolized, they none the less remain in the environment. We know that pesticides compounds are an essential part of our modern production technology, and at this point in time it is impossible for us to continue without using them. However, we are at a point in time where it is absolutely essential that we weigh the benefits and the hazards to achieve a favorable balance. In order to make this weighing and to formulate this decision, it is essential that we gain more knowledge on the decomposition and metabolism particularly of the chlorinated pesticides.

The second principal group of insecticides consists of the organophosphates. We will talk about four groups of these compounds and point out the differences in structure. From the chemical standpoint, organophosphates are named as esters of phosphoric acid. However, in the handling of these complex molecules, the naming system often breaks down and we find exceptions to this general rule. In the names of organic phosphates, you will often find a group preceded by a capitol O or a capitol S; in addition, in some organophosphates and in many of the other groups of compounds which we will look at, we often find a capitol N used. The O in this case does not mean the old classical organic chemistry ortho, as it is a capitol O. The O simply means that a particular group is tied through an oxygen bridge. S means that the group is tied through a sulfur bridge. Capitol N indicates that we have groups attached to a nitrogen. Generally speaking, this is the replacement of the hydrogens on the amino group.

The first of the four groups which we will consider is the alkene group, often referred to as vinyl or similar type compounds. The first example of this is the compound bidrin, which has, in my opinion, a rather atypical structure. By atypical, I am referring to the bonding between the phosphorus and oxygen, which in this molecule appears to be a true double bond. This is rather atypical in organophosphates, in that we generally find the bonding at this position designated by an arrow between the two elements, indicating a coordinate covalent bond. The next compound, dichlorvos, represents a typical structure. Most phosphates, perhaps all organophosphates, have oxygen or sulfur attached to the phosphorus by a coordinate covalent bond. In this type of bonding, the phosphorus contributes all the electrons. The determination of bond angles and distances has proven the existence of the coordinate covalent bond. This is, in effect, a double bond from the standpoint of valence. Such bonding arrangement is responsible for the extreme toxicity of most organophosphates. Oxygen bonded to phosphorus in this manner draws electrons and creates an extremely positive phosphorus, resulting in a compound which is very soluble, reactive, and toxic.

Phosphates include both true phosphates and phosphonates. True phosphates are those compounds which do not have a direct carbon-phosphorus bond. That is, the phosphorus is separated from the carbons by an oxygen or sulfur. These compounds are referred to as phosphorates or phosphorothioates, depending upon whether or not they contain sulfur. Phosphonates are those organophosphates which have a direct carbon-phosphorus bond. These compounds are named phosphonates or phosphonothioates, again depending upon whether or not they contain sulfur. Bidrin and dichlorvos are phosphates. Trichlorofon is an example of a phosphonate. Trichlorofon fits the category only as a "similar to" the vinyl group. The manufacturer fouled up the typical vinyl grouping by saturating the carbons with a hydroxyl and an extra chlorine group. None the less, trichlorofon is characteristically a vinyl type structure. A second interesting characteristic of this compound is that it is hydrolized to chloralhydrate. Chloralhydrate is a compound which you can pick up at most any bar by needling the bartender; "knock out" drops.

The second group of organophosphate insecticides is the aliphatic or alkane type. The compound dimethoate is a good example of this group. Pay particularly close attention to the side chain group attached through the second sulfur atom. The particular group of interest here is the CONH group, referred to as a carbamoyl. It is also referred to, at times, as a peptide linkage which you probably recall from amino acid groups as they combine to form proteins. This carbamoyl group is characteristically similar to a carbonyl, except that it results from carbamic acid rather than carbonic acid. So, we have in this compound a little of what we are discussing now and a bit of what we will be discussing later, the carbamates. This is also an example of a phosphorothioate, or more correctly, a phosphorodithioate, since we have two sulfurs in the molecule. Dimethoate, often called cygon, is not terribly toxic and none of the parent compound remains as a residue. It is readily decomposed by hydrolysis. The second compound, malathion, has experienced a tremendous increase in use in the last few years. We have been told that it is not particularly toxic, but we have had some difficulties with it. I suspect these were concerned with large concentrations. Malathion does oxidize to malaoxon; that is, the sulfur indicated by the arrow bond to phosphorus, is replaced by oxygen. Malaoxon is more toxic than malathion because the phosphorus becomes more positive, is more soluble, more reactive, and thus is more toxic. The fact that malathion is generally considered to be rather non-toxic indicates that the positive phosphorus is in some way modulated. The diester grouping of the side chain is interesting and may have something to do with the reduced toxicity of this molecule. The third compound in this series is phorate or thimet. This compound contains two rather interesting points; one, the name. We might have a tendency to look at it with three sulfurs and to name it as a phosphorotrithioate. Actually, we consider the thioethyl group on the end of the side chain, and name the compound as a dithioate. The second interesting point also deals with that third sulfur sulfoxide, that is one oxygen attached, or a sulfone, two oxygens. The oxidation to a sulfoxide renders this compound considerably more toxic than the parent. This is also true of any compound so constructed that a sulfur can be oxidized to a sulfoxide or a sulfone. This oxidation can take place on any sulfur which is not attached directly to the phosphorus. In other words, if we consider the phosphorus-sulfur-CH_2 linkage, such oxidation cannot occur. This statement is also true of the coordinate bonded sulfur indicated by the arrow. The second sulfur located between the two carbons will oxidize to the more toxic compound.

The third type of organophosphorus insecticide consists of the aryl, or aromatic types. In essence, these compounds are acid anhydrides of phosphoric acid and phenols. Some of the phenols perhaps may be a bit difficult to recognize since they are also substituted. In the reaction of phosphoric acid and phenol, water is split out, forming an acid anhydride. Acid anhydrides are notoriously easily hydrolized; and as they are hydrolized, they are once again returned to phosphoric acid, howbeit substituted, and phenols, the alcoholic moiety. This phenol, or alcohol, is generally also substituted. This hydrolysis, and the release of phenols into the environment, substituted or not, is a point in my contention, previously stated, that we are literally saturating the environment with phenolic compounds. These phenolic compounds require a little closer attention than we have been giving them.

Parathion is an extremely toxic compound and is readily converted to paraoxon, which is, of course, more toxic than the parent. As the oxygen analog, the phosphorus again becomes more positive, more soluble, and more reactive. This is probably the reason for the increased toxicity. Parathion, as you know, is readily decomposed and metabolized.

The second compound of the aromatic phosphates is diazinon. Diazinon is perhaps one of the least toxic of the organophosphates. The bonding between the phosphorus and sulfur does appear to be a true double bond. In the case of a true double bond, sulfur would also contribute electrons to the union and thus the phosphorus would be somewhat less positive and less reactive than in the case of a coordinate covalent bond. The stability of this compound is emphasized in that diazinon is the most persistent of the organophosphates. Diazinon contains a diazo-type ring structure, which may be a potentially hazardous environmental contaminate.

The compound methyl parathion has a slight structural modification from parathion, methyl groups on the ring instead of ethyl. The reactions, utilization, and toxicity of this compound are quite similar to parathion.

Ronnel is a chlorinated phenolic phosphate, useful in qualitative analysis. Having chlorine, sulfur, and phosphorus moieties, we can use diverse analytical methods and readily establish positive identification. Guthion is a rather toxic compound which contains a diazo structure in the aromatic side chain. Actually, it is referred to as a triazo structure and is named as a benzotriazine. The last compound that we will look at in this group is EPN. The letters EPN stand for O-ethyl-O-paranitrophenyl phenyl-phosphonothioate. The name indicates, and you will recognize from the structure, that this is again a phosphonate. That is, the phenyl group on the left is tied directly to the phosphorus, and the bond is between the phosphorus and the carbon. EPN, as parathion, and methyl parathion, is hydrolized to paranitro phenol. The fourth and final group in the organophosphate insecticides consists of TEPP. Tetraethyl pyrophosphate is a rather innocent looking compound, but as I am sure you all know, is an extremely toxic one. I doubt that tetraethyl pyrophosphate has any appreciable hazard to the applicator and to anyone accidentally exposed. TEPP unfortunately is being used even today but in rather small quantities, fortunately, for the most part, by rather well oriented pest control operators.

Carbamates are the third group of insecticides of particular importance at the present time. Carbamates are named as esters of carbamic acids and their structures contain the carbamate stem OCONH. Carbamates are reported to have low mammalian toxicity, but there are some instances where they can be, and have been, made extremely toxic by reaction. Carbamates are surface sensitizing; there have been cases of dermatitis resulting from the use of carbamate insecticides. They produce some questionably hazardous decomposition products and, certainly at this point in time, need a considerable amount of investigation. Carbamates are utilized as insecticides, herbicides, and fungicides. This doesn't mean to imply that the same compound can do all three jobs, but there are members within this chemical species which can do one or the other, and in some instances, more than one. I've classified the carbamates as monomethyl, or n-methyl, and dimethyl, or n,n-dimethyl. N-methyl or n,n-dimethyl refers to the substitution of the nitrogen on the carbamate matrix. As we look at some of the structures, I can point out much more easily just what I am referring to. The monomethyl compounds are the most labile; they are usually solids, probably due to the hydrogen bonding on the NH group. We will discuss the reactions more completely later.

The first compound which we look at, sevin, one of the monomethyls, is said to be a reasonably safe material. There is considerable investigation currently in progress on the metabolism of this agent. As I indicated, these are esters of carbamic acid; that is, carbamic acid and an alcohol. The compound sevin contains a rather complex alcohol, naphthol.

The second compound of interest is the one referred to as temik. Temik is basically an oxime. The carbamate moiety on the right is mono-substituted by a methyl group, thus a monomethyl carbamate. On the left of this structure you will notice that once again we have a sulfur positioned between two carbon atoms. This sulfur oxidizes rather readily to a sulfoxide, that is the addition of one oxygen, and eventually to a sulfone, the addition of two oxygens. As the sulfoxide, the compound temik, which is referred to as temik sulfoxide, is extremely toxic. The sulfone, that is, temik sulfone, is not quite as toxic but still more so than the parent compound. While the parent compound may not be particularly toxic, it is readily and easily converted to a toxic compound.

The second group of carbamates, the dimethyl, are much more stable to heat and light and are usually liquid. Both their stability and the fact that they are liquid appear to be associated with hydrogen bonding of the nitrogen or perhaps I should say the lack of hydrogen bonding. The lack of hydrogen bonding reduces the rigidity of the compound with the resulting liquid state. In addition, methyl saturation (not easily hydrolyzed) of the nitrogen enhances stability. The compound dimetilan is an example of this group. The carbamate matrix is on the right; however, it doesn't look greatly different from the left side, which is referred to as a carbamoyl.

The next compound is desin, an example of a carbonate, and the only one that is used to any extent, to the best of my knowledge. I simply wanted to call this compound to your attention and to point out the similarity between the carbamoyl and the carbonyl groups. In other words, if we added a nitrogen or amino group to a carbonyl, we would find ourselves with a carbamoyl or a carbamate structure.

There are many other insecticides compounds which could be discussed; however, the only ones that we will even mention at this point are the arsonates. This group contains some rather potent and toxic materials which are not currently being used to any great extent as insecticides. I trust we will soon be referring to them only out of historical respect.

The second use group of pesticides which we will consider is herbicides. Herbicides, as I indicated to you in the beginning, are not well understood, at the present time. Their potential, the toxicity of the parent compound in many cases, and the decomposition products, and metabolites of many of the herbicides need to be studied extensively. We have experienced a great deal of controversy and hopefully some interest over the use of herbicides in Southeast Asia. There are those who are concerned about their long-term effect on the ecosystem.

There are certain chemical species of herbicides which may be potentially dangerous, and in this discussion we will endeavor to indicate those which could produce potentially hazardous decomposition products. The first herbicide compound we will consider is CIPC, chloroisopropylcarbamate. Looking at the substituted groups on the amino of the carbamate matrix, we notice a mono substitution; however, it is not a mono methyl as we found in the insecticides. In this case it is a mono substitution by an aromatic component; a chlorinated phenol. The reactions on this compound are similar to those of insecticidal carbamates, with the exception that hydrolysis, in this case, has been shown to yield analine, at least in soil.

The second compound, ordram, is a thiocarbamate which we can consider to have a seven member ring. We can visualise this compound as disubstituted carbamate nitrogen. The carbamate matrix includes one oxygen and one sulfur rather than the two oxygen atoms with which we are familiar. Ordram to some extent is similar to temik in that the sulfur can be oxidised to a sulfoxide or sulfone and as such will be considerably more toxic.

A third species of herbicides is the substitutes ureas. Monuron is an example of a urea herbicide and is a reasonably popular agent. I'd like to call your attention to the urea stem in this case and to make sure that you are able to differentiate between the urea and the carbamate matrices. You recall that the carbamate matrix results from carbamic acid which is NHCOOH. Consequently, the carbamate stem is a substituted NH_2COO. Urea, on the other hand, is NH_2CONH_2, and here it is substituted by a ring structure on the left which looks very similar to the compound CIPC. However, on the right side we have lost the acid radical and returned to a substituted NH_2 as we would find in urea. These compounds are named as mono or dimethyl urea with the substituted products preceding that name. Thus, for monuron we have 3,4,chlorophenyl-1,1 dimethyl urea.

The fourth group of herbicides consist of the metallo-organics. Methane arsonic acid is probably the best known, or was the best known until recently, of the metalo-organics. It is usually applied as a sodium salt and is a rather simple straight chain material. Cacodylic acid, perhaps because of the furor over Viet Nam, is now the best known of the metallo-organic herbicides. The chemical name of this material is dimethyl arsenic acid. It is an excellent herbicide and the toxicity is very low, a point which we need to remember in this argument over whether we should kill vegetation with herbicides or people with guns, bombs, and booby traps. The toxicity of this material is in the area of about a gram per kilogram.

The fifth group of herbicides consists of the inorganics, such as arsenic trioxide and arsenic pentoxide. Arsenic pentoxide in particular is very toxic and has a tendency to persist for a long period of time in the soil. These compounds are comparatively simple straight chain inorganics.

The sixth and seventh group of herbicides consists of the triazoles and the triazines. Amino triazole, amitrole, is a very reactive material and has been known to be goitrogenic in animals on continued feeding of relatively high concentrations. This is the one that was involved in the famous cranberry affair which some people have indicated was only political. None the less, it is not particularly difficult to appreciate the concern, be it true or sham, because of the triazo ring. Additional information that it is carcinogenic in large concentration is perhaps some defense of the cranberry incident. Simazine is an example of a symmetrical triazine. The azo ring structure does indicate some cause for concern with this particular material; however, the compound, as appears to be true of all symmetrical triazines, is very stable.

Dinitro-orthocresol (DNOC) is an example of phenolic herbicides, and while it may be a bit extreme, I believe it presents a potential problem with phenolic compounds. DNOC is, of course, a very toxic material and it is carcinogenic. It is an excellent weed control agent, an old timer, but is being replaced by herbicides which are probably just as effective and not quite as hazardous. An interesting point on DNOC is that a number of years ago it was being prescribed as a weight control agent. As a matter of fact, it was responsible for the loss of several pretty girls until its carcinogenicity was finally realized.

The ninth group of herbicides, the aniline compounds, can be represented by trifluralin. It is an interesting compound because it is one of the few fluorine pesticides in use. While I have considerable concern about analine compounds, this particular one seems to be of little concern since it is relatively nontoxic and appears to be relatively stable. Actually, only one propyl group from the nitrogen is lost and the resulting product has a very low toxicity. The second compound in this group is the one referred to as stam. Another name for it is propanyl, or 3,4,dichloro propionanilide. This compound readily hydrolyzes to dichloro analin and is a compound worth worrying about. More recently it has been shown that the analine compound in the presence of certain soil micro-organism is further degraded to a diazo compound, also worth worrying about.

The tenth group, the amides, is represented here by diphenamid. It is a dimethyl diphenyl acetamide. The compound is relatively nontoxic and is apparently removed from the body as a conjugate found in urine. Apparently, the conjugation takes place through the nitrogen with glucose or possibly other sugars. The amide group, of course, is the $CONH_2$; the hydrogens on the nitrogen having been replaced by two methyl groups. Differentiate this group from the urea compounds which are NH_2CONH_2 with substitutions on the nitrogen. Also differentiate this from the carbamates which are $OOCNH_2$ with substitutions on the nitrogen.

The eleventh and final group of the herbicides which we will consider is the organic acids. These are very persistent compounds howbeit they are relatively nontoxic. Relative toxicity, of course, is sometimes a bit difficult to visualize. Perhaps one of the best known of the organic acid herbicides is 2,4-D, and contrary to what we sometimes hear, 2,4-D is more toxic than DDT. It will be interesting when we find out just how 2,4-D and DDT compare as to their potential toxicity. Certain formulations of 2,4-D have also been found to be contaminated with the very toxic chlorodioins. Benzoic acid is not a particularly good herbicide, but it is a good model since it is reacted with chlorine, methyl groups, and amines, to produce effective herbicides. Benzoic acid itself is relatively nontoxic; it is about as toxic as table salt. Dacthal is a good example of the modification of benzoic acid to produce a useful and relatively safe herbicide. It is substituted with both chlorine and methyl groups. The herbicide dalapon is an example of a straight chain or aliphatic organic acid.

The third and final group of pesticide compounds which we would like to consider are the fungicides. The toxicity of fungicides are generally low as compared to other pesticides and to many drugs; there are, of course, exceptions to this rule. Our brief discussion will center on a very few of a very many chemical species utilized as fungicides. The first group of fungicides for consideration are the heavy metals. Many of these heavy metals are nontoxic and a few of them may actually be healthful although this is certainly open to question. Some of the most toxic of the heavy metal fungicides are the tin complexes currently in the experimental stage. Chromium and cadmium complexes are primarily an occupational problem due mostly to inhalation. Mercury is perhaps the most dangerous of those actually in use. Mercury is used in seed treatment where it constitutes a dust hazard particularly to the applicators and those occupationally exposed to the seed. Mercury functions by combining with the negative centers of enzymes such as the SH and carboxyl groups or by displacement of metals essential to the functions of certain enzymes.

The second group of fungicide compounds are those referred to as the organometallics. If you recall, we had a few of the organometallic compounds used as herbicides, the principal one being cacodylic acid. Bioquin is an example of an organometallic fungicide or chemically, 8 copper quinolinolate. Bioquin is an example of a chelate compound; that is, a compound which will hold a metal between two partially negatively charged centers, in this case, the nitrogens.

Organohalides are the next chemical group, useful as fungicidal agents. You recall that we have discussed organohalides all through this presentation. Organohalides, chiefly organochlorines, are the best known and most used insecticides. We also found that a number of herbicide agents are organohalides; organochlorines. The organohalide fungicides are the most potentially dangerous group. One good example of this group is parachloronitro benzene of PCNB. It is sold under the trade name of Terrachlor, which is a good indication of its potentially dangerous structure. You will notice that it has a nitro group on one end and a chlorine on the other. The principal potential hazard associated with this fungicide is the fact that it can be easily reduced to analin. Pentachlorophenol is a second example of an organohalide fungicide and is particularly interesting in that it is a phenol generously substituted with chlorine. This particular one is used as a wood preservative and it seems to be omnipresent. It is a good bet that PCP is present in human tissues all over the world. As I indicated, this is a phenol; it is readily taken into the system and is excreted in the urine, unchanged.

The fourth group of fungicide compounds are the quinones. Quinones have a very low toxicity; however, they are irritating to the skin and are mild oxidizing agents. Chloranil is a typical substituted quinone, substituted in this case with chlorine. Dichlone, the second of this series, looks very much like a quinone, substituted on the left by an aromatic and on the right with chlorine. This particular fungicide is chemically related to vitamin K and, as a matter of fact, has some vitamin K activity. This is referred to as a napthoquinone, actually 2,3,dichloro-5,6-napthoquinone.

The fifth chemical species of fungicides is the triazines. You recall we had a triazine herbicide, simazine. We are now looking at the triazine fungicide, dyrene, an example of a triazine which has both herbicidal and fungicidal activity. The molecule itself is quite similar to that of simazine showing the same symmetrical triazine ring. Dyrene can be hydrolyzed to a chloro-substituted analine.

Elemental sulfur is the sixth group used as fungicides. This is an old timer which is still being used to some extent. I suppose everybody knows about the use of elemental sulfur as a fungicide. So far as we know, we do not have any problems from the use of elemental sulfur except that slight discomfort may arise from its oxidation products. Certainly from the analytical standpoint more than slight discomfort arises from oxidation products of sulfur which may be in samples and indicate other compounds for which we are attempting to analyze.

Organosulfur compounds are the seventh group of fungicides and probably the most important from the standpoint of use. Thiram is perhaps the best example of an organosulfur fungicide. This is a very good fungicide and used fairly heavily in seed treatments and on some plants. Thiram is an example of a chelating compound as we shall see a bit later on.

Substituted imides constitute the eighth group of fungicides, one good example of which is captan. Captan is probably second in use to thiram, and it is not toxic in so far as we know. It is fairly highly substituted with chlorine and could conceivably concentrate in human tissues.

A final group of fungicides are the thiocarbamates; these are probably the major group of fungicidal compounds. Thiocarbamates are about as toxic as 2,4-D. There are two subcategories of thiocarbamates; first the dialkyldithiocarbamates, represented here by the compound ferbam. Ferbam, ferric dimethyl dithiocarbamate incorporates an iron or ferric atom in the compound. A similar compound is ziram which contains a zinc atom rather than the feric.

The second category, alkylenbisdithiocarbamates, exemplified by the compound zineb, or zincethylenebisdithio carbamate. A second compound, nabam, contains disodium, or two sodiums in a molecule in place of the zinc; and maneb contains manganese rather than zinc.

Initially, I indicated that we would talk about the reactions of some of these type compounds. I would like to preface these remarks by pointing out that we have selected a representative compound from each particular chemical. Needless to say, there are a tremendous number of exceptions to the reactions of different compounds within a chemical species. Consequently, when we go much beyond the more stable and persistent chlorinated organic compounds, we will find a tremendous difference in the reactions between compounds within a given species. We are not going to discuss the more classical reactions but rather limit our discussion to some of those conditions and produce products conceivably related to health.

When we consider the reactions of DDT, we can understand why this compound is a persistent material. DDT is stable to reduction and oxidation; it is dechlorinated at high temperatures, but these are rather extreme temperatures. DDT is hydrolyzed under alkaline conditions to the compound DDE, which we have previously indicated is a nontoxic material. In metabolism DDT is also hydrolyzed to DDE, and this product accumulates in human tissue. The accumulation of DDE is a fair index of extended exposure to DDT. DDT is also hydrolyzed to the compound DDA found in the urine and used as an index of recent exposure to DDT. It has also been reported that in the presence of iron porphyrin complexes, DDT is dechlorinated to DDD.

Aldrin is quite stable to heat, dilute acids, and alkaline hydrolysis. Aldrin, as we indicated before, is epoxidized either in vitro or vivo to the compound dieldrin. Thus, aldrin is not persistent as the parent compound and is found almost entirely in human and animal tissue and plants as dieldrin. To a large extent, it is found in the ecosystem as dieldrin rather than the parent compound.

In benzenehexachloride, lindane exemplified the stability of this class to oxidation, light, heat, and acids. Lindane is dechlorinated by alkaline hydrolysis to trichlorobenzenes. Lindane is quite stable in metabolism but rather than concentrate in human tissues, lindane is rapidly excreted.

The fumigant methyl bromide is stable to heat, oxidation, reduction, and hydrolysis. Under metabolism by both plants and animals, methyl bromide has a tendency to brominate amino acids, particularly the amino acid histadine with the production of a 1-bromo and a 1,3 dibromo histadine. Inorganic bromine residues remain, particularly in plant tissue and possibly in animal tissue, as a result of the methylation of hydroxyl, carboxyl, and amino groups. Unreacted methyl bromide is not persistent since the compound is volatile.

The organophosphate parathion decomposes at a high temperature with the evolution of gas. Parathion is hydrolyzed to paranitrophenol and substituted phosphoric acids, alkyl phosphates. As indicated previously, parathion is easily oxidized to the analog paraoxon, which is considerably more toxic than the parent compound because oxygen increases the positive characteristic of phosphorus, thus making the compound more soluble, more reactive, and more toxic. Under metabolic conditions, parathion is also hydrolyzed to paranitrophenol. Parathion, when oxidized to paraoxon, reacts with the enzyme cholinesterase, which is the mode of action of parathion.

The carbamate sevin or carbaryl is decomposed by both alkaline hydrolysis and heat to methyl isocyanate and 1-napthol. This is a class reaction for all carbamates, which in the presence of alkaline hydrolysis or heat, decompose to methyl isocyanate and the corresponding alcohol. Carbaryl is stable to oxidation and reduction. Under alkaline conditions, sevin is metabolically hydrolyzed to one napthol and probably methyl isocyanate, which has not been found. One napthol reacts with carbohydrates to form conjugated structures which are found in the urine. Carbamates also inhibit the activity of the enzyme, cholinesterase.

The fungicide thiram, as previously indicated, is a chelating agent and undoubtedly its mode of action is by chelation of the essential metal ion of certain enzymes. This chelation occurs either in vitro or vivo. Thiram is hydrolyzed under acid conditions to copper, carbon disulfide, and either methyl or dimethyl amines. Thiram is stable to oxidation, reduction, and heat. Under metabolism, thiram is also hydrolyzed under acid conditions to carbondisulfide and amines and can also be involved in mixed disulfide reactions of proteins.

Amino triazole is oxidized, both in vitro and in vivo, to a dizo product, which is probably responsible for its carcinogenicity. It is stable to light and hydrolysis but conjugates with amino acids and is excreted as the amino acid complex.

Stability is the key word for 2,4-D. This compound is stable to heat, oxidation, and reductions, but is converted to a dichlorophenol by ultraviolet light and halogen acids. Consequently, 2,4-D should be very persistent in the ecosystem. On metabolism, 2,4-D conjugates with glucose and is excreted as such in the urine.

In this brief period of time we have emphasized the matrix and reactive groups of type compounds of the most prominent pesticides. A limited number of reactions have been discussed as well as some of the handles available for analysis. It is my hope that you will appreciate the diverse nature of pesticide chemistry, that you will be able to distinguish between the various chemical species involved and that we will all take steps to minimize the potential hazards of chemical pesticides.

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Toxicology of Pesticides: Introduction

August Curley

I. Introduction

    A. Toxic hazards in the human environment

        1. Extraneous
        2. Natural

    B. The study of chemical-biologic mechanisms- "the biochemical lesion".

II. Structure and reactivity or activity relationship

    A. The chemical structure

        1. Chlorinated hydrocarbons
        2. Organophosphate esters and carbamates
        3. Metals - ionic or alkylated

    B. Reactivity or activity and/or binding of the toxic chemical to cell constituents

III. Mechanisms of toxicity - modes of action

    A. Reactions with cellular constituents or organs

        1. Reversible binding
        2. Covalent binding

    B. Interference with vital metabolic pathways

    C. Protective biochemical mechanisms

        1. Drug metabolizing enzymes
        2. Lipid solubilities

    D. Systems for detecting and measuring physiological changes

        1. Effects on central nervous system - ion imbalances
        2. Behavior
        3. Pathology
        4. Immunity and sensitivity
        5. Epidemiology

IV. Summary

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PESTICIDES OF PUBLIC HEALTH SIGNIFICANCE

Harold G. Scott

Tens of thousands of chemicals have been evaluated for insect-, rodent-, weed-, and fungus-control. Hundreds of these are in daily use in the pest control field, and additional materials are being developed continually. As a result, even individuals engaged in pesticide research find it difficult to stay abreast of this vast and rapidly changing field.

Essential to comprehension of pesticides is an organized knowledge so unfamiliar chemicals can be associated with known materials and present background of knowledge can be used as a basis for understanding the new chemicals. As advances are made in pesticide knowledge, greater understanding of their toxicity to mammals is obtained. It should be emphasized, that degree of toxicity cannot be determined by the relative position of the pesticides in the charts. With any pesticide, all necessary safety precautions should be taken.

The following four charts present 350 of the most commonly used pest control materials in a practical system based upon a combination of chemical structure and pest control effect.

GLOSSARY OF TERMS AS USED ON THE CHARTS

ALGICIDE - chemical which kills algae

ANTICOAGULANT - rodenticide which kills by interfering with blood clotting

ATTRACTANT - chemical which draws an animal to a place

AUXILIARY - chemical without pest control effect used in pesticide formulation

BINDER - a substance used to hold rodenticide bait material together

BUFFER - substance added to herbicides to control acid-alkalai balance; protects herbicide from deterioration; enhances herbicidal effect

CONTACT POISON - insecticide which kills upon contacting the outer body surface of an insect

DEODORANT - material masking or destroying odor

EMETIC - chemical causing vomiting; added to rodenticides for safety

EMULSIFIER - chemical which suspends a pesticidal solution in water

FUMIGANT - pesticide which kills upon being inhaled

FUNGICIDE - chemical which kills fungi

HERBICIDE - chemical which kills weeds and other plants

IMPREGNANT - insecticide or repellent infused into clothing or other material

INHIBITOR - chemical which prevents insects from detoxifying an insecticide

INORGANIC - chemical compound not containing carbon

INSECTICIDE - chemical which kills insects and related animals

MOLD INHIBITOR - chemical which prevents mold development in rodenticide baits

NATURAL - found in nature, not synthesized by man

NON-SELECTIVE - kills all types of plants

NON-SUBSTITUTED - organic compound made up of only carbon and hydrogen and sometimes oxygen

ORGANIC - chemical compound containing carbon

REPELLENT - chemical which keeps an animal away from an individual, object or area

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

RODENTICIDE - chemical which kills rodents and related animals

SELECTIVE - kills only certain types of plants; does not harm other types

SOLVENT - liquid used for dissolving chemicals

SPREADER - substance which distributes pest control chemical through a greater volume

STERILANT - herbicide which kills all plant life in soil

STOMACH POISON - insecticide which kills upon being eaten

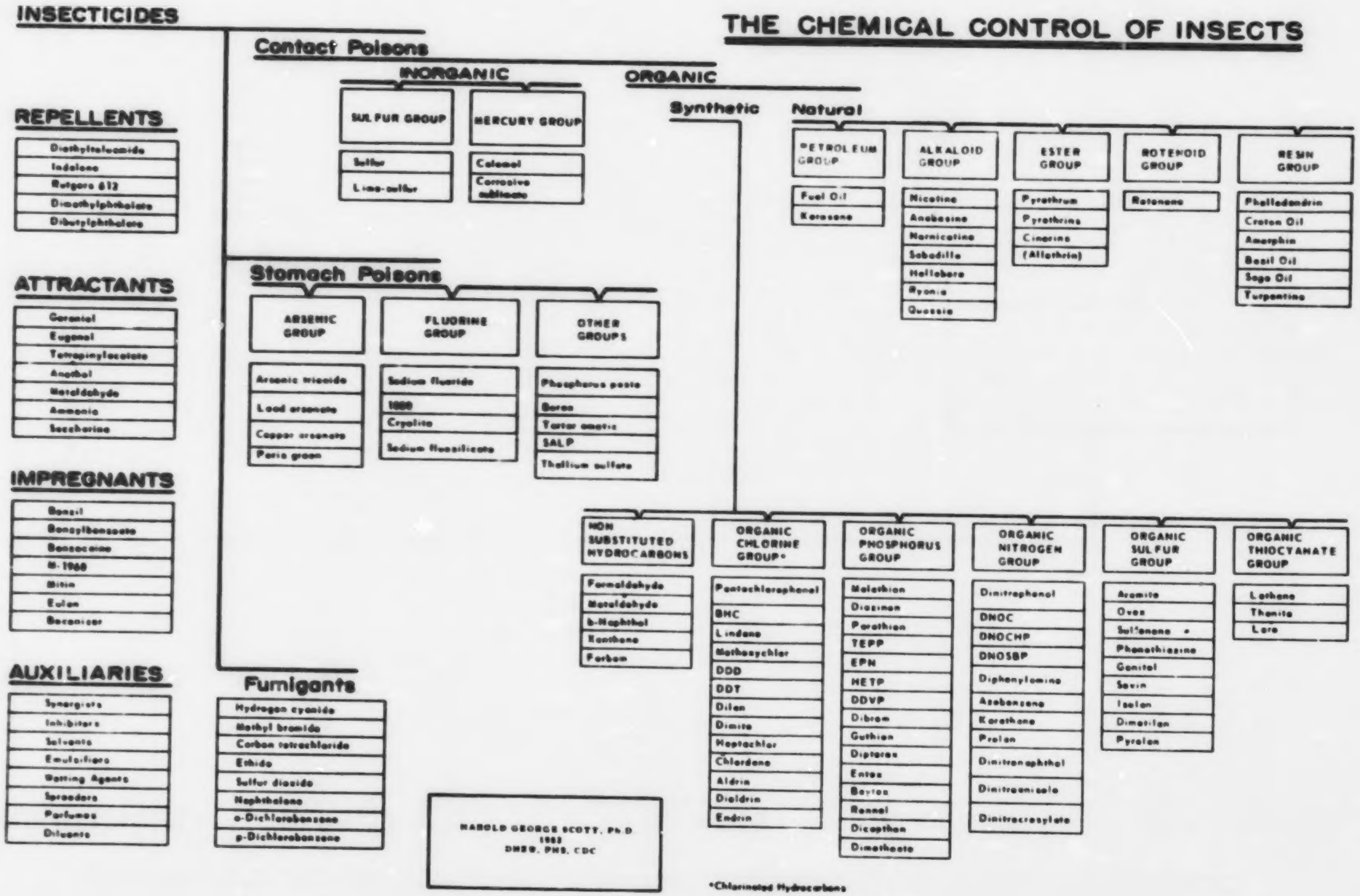
SYNERGIST - chemical without pest control effect which enhances the effectiveness of a pest control chemical

SYNTHETIC - manufactured by man; not found in nature

WETTING AGENT - chemical which helps suspend a pesticidal dust in water

NOTE: Use of trade names does not indicate endorsement by the Public Health Service. Incorporation of chemicals in these charts does not necessarily imply that the Communicable Disease Center has evaluated all of these materials. For example, herbicides and economic fungicides have been little studied by the Center due to their relatively minor role in communicable disease control.

THE CHEMICAL CONTROL OF INSECTS

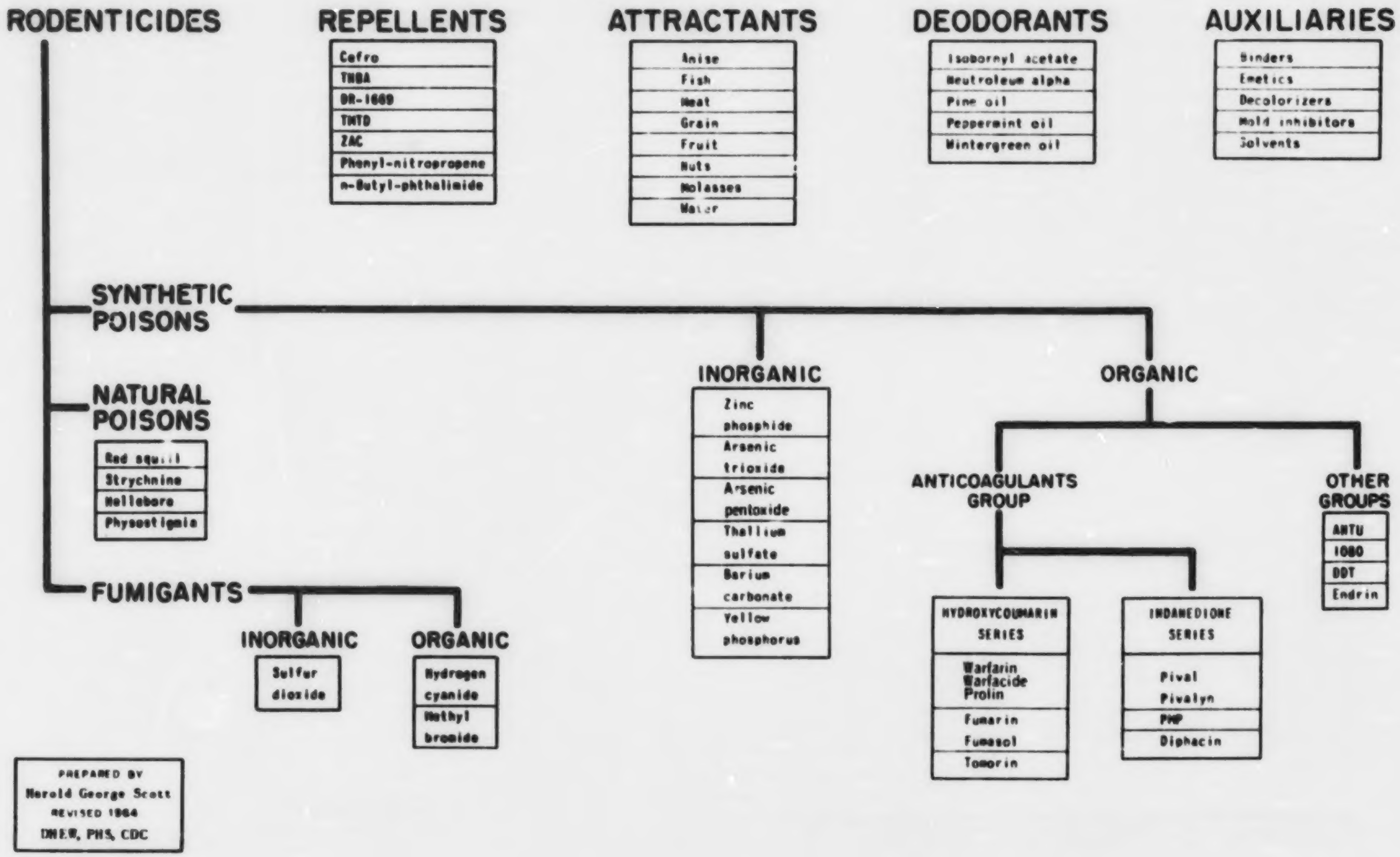


- **INSECTICIDES**
  - **Contact Poisons**
    - **INORGANIC**
      - SULFUR GROUP
        - Sulfur
        - Lime-sulfur
      - MERCURY GROUP
        - Calomel
        - Corrosive sublimate
    - **ORGANIC**
      - **Synthetic**
        - NON SUBSTITUTED HYDROCARBONS
          - Formaldehyde
          - Metaldehyde
          - b-Naphthol
          - Xanthone
          - Ferbam
        - ORGANIC CHLORINE GROUP*
          - Pentachlorophenol
          - BHC
          - Lindane
          - Methoxychlor
          - DDD
          - DDT
          - Dilan
          - Dimite
          - Heptachlor
          - Chlordane
          - Aldrin
          - Dieldrin
          - Endrin
        - ORGANIC PHOSPHORUS GROUP
          - Malathion
          - Diazinon
          - Parathion
          - TEPP
          - EPN
          - HETP
          - DDVP
          - Dibrom
          - Guthion
          - Dipterex
          - Entex
          - Baytex
          - Ronnel
          - Dicapthon
          - Dimethoate
        - ORGANIC NITROGEN GROUP
          - Dinitrophenol
          - DNOC
          - DNOCHP
          - DNOSBP
          - Diphenylamine
          - Azobenzene
          - Karathane
          - Prolan
          - Dinitronaphthol
          - Dinitroanisole
          - Dinitrocresylate
        - ORGANIC SULFUR GROUP
          - Aramite
          - Ovex
          - Sulfenone
          - Phenothiazine
          - Genitol
          - Sevin
          - Isolan
          - Dimetilan
          - Pyrolan
        - ORGANIC THIOCYANATE GROUP
          - Lethane
          - Thanite
          - Loro
      - **Natural**
        - PETROLEUM GROUP
          - Fuel Oil
          - Kerosene
        - ALKALOID GROUP
          - Nicotine
          - Anabasine
          - Nornicotine
          - Sabadilla
          - Hellebore
          - Ryania
          - Quassia
        - ESTER GROUP
          - Pyrethrum
          - Pyrethrins
          - Cinerins
          - (Allethrin)
        - ROTENOID GROUP
          - Rotenone
        - RESIN GROUP
          - Phellodendrin
          - Croton Oil
          - Amorphin
          - Basil Oil
          - Sage Oil
          - Turpentine
  - **Stomach Poisons**
    - ARSENIC GROUP
      - Arsenic trioxide
      - Lead arsenate
      - Copper arsenate
      - Paris green
    - FLUORINE GROUP
      - Sodium fluoride
      - 1080
      - Cryolite
      - Sodium fluosilicate
    - OTHER GROUPS
      - Phosphorus paste
      - Borax
      - Tartar emetic
      - SALP
      - Thallium sulfate
  - **Fumigants**
    - Hydrogen cyanide
    - Methyl bromide
    - Carbon tetrachloride
    - Ethide
    - Sulfur dioxide
    - Naphthalene
    - o-Dichlorobenzene
    - p-Dichlorobenzene
- **REPELLENTS**
  - Diethyltoluamide
  - Indalone
  - Rutgers 612
  - Dimethylphthalate
  - Dibutylphthalate
- **ATTRACTANTS**
  - Geraniol
  - Eugenol
  - Tetrapinylacetate
  - Anethol
  - Metaldehyde
  - Ammonia
  - Saccharine
- **IMPREGNANTS**
  - Benzil
  - Benzylbenzoate
  - Benzocaine
  - M-1960
  - Mitin
  - Eulan
  - Boconizer
- **AUXILIARIES**
  - Synergists
  - Inhibitors
  - Solvents
  - Emulsifiers
  - Wetting Agents
  - Spreaders
  - Perfumes
  - Diluents

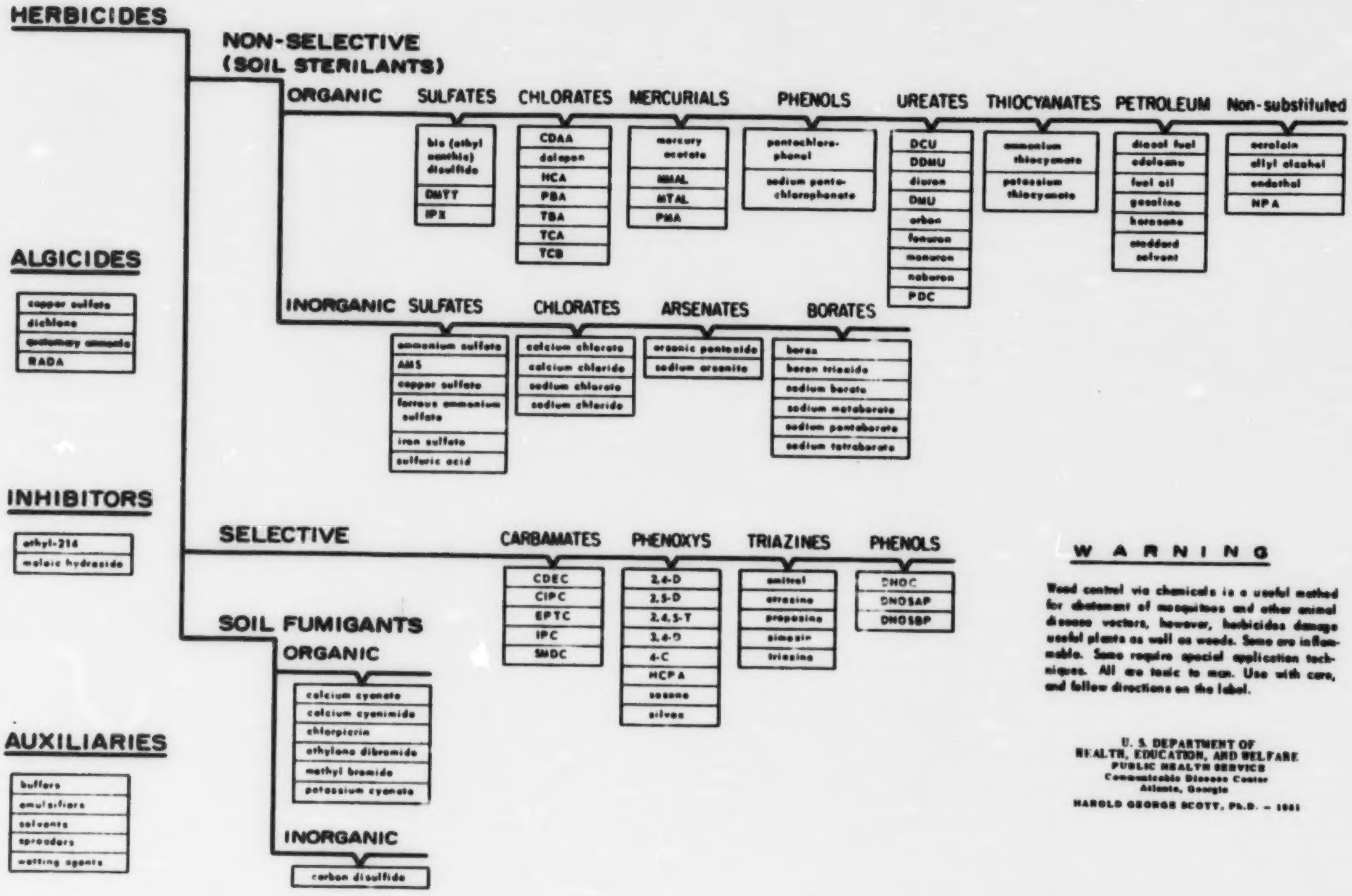
HAROLD GEORGE SCOTT, Ph.D
1963
DHEW, PHS, CDC

*Chlorinated Hydrocarbons

THE CHEMICAL CONTROL OF RODENTS


RODENTICIDES
SYNTHETIC POISONS
INORGANIC
Zinc phosphide
Arsenic trioxide
Arsenic pentoxide
Thallium sulfate
Barium carbonate
Yellow phosphorus
ORGANIC
ANTICOAGULANTS GROUP
HYDROXYCOUMARIN SERIES
Warfarin
Warfacide
Prolin
Fumarin
Fumasol
Tomorin
INDANEDIONE SERIES
Pival
Pivalyn
PMP
Diphacin
OTHER GROUPS
ANTU
1080
DDT
Endrin
NATURAL POISONS
Red squill
Strychnine
Hellebore
Physostigmia
FUMIGANTS
INORGANIC
Sulfur dioxide
ORGANIC
Hydrogen cyanide
Methyl bromide
REPELLENTS
Cefro
TNBA
DR-1669
TMTD
ZAC
Phenyl-nitropropene
n-Butyl-phthalimide
ATTRACTANTS
Anise
Fish
Meat
Grain
Fruit
Nuts
Molasses
Water
DEODORANTS
Isobornyl acetate
Neutroleum alpha
Pine oil
Peppermint oil
Wintergreen oil
AUXILIARIES
Binders
Emetics
Decolorizers
Mold inhibitors
Solvents

PREPARED BY
Harold George Scott
REVISED 1964
DHEW, PHS, CDC


HERBICIDES
NON-SELECTIVE
(SOIL STERILANTS)
ORGANIC
SULFATES
bis (ethyl xanthic) disulfide
DMTT
IPX
CHLORATES
CDAA
dalapon
HCA
PBA
TBA
TCA
TCB
MERCURIALS
mercury acetate
MMAL
MTAL
PMA
PHENOLS
pentachlorophenol
sodium pentachlorophenate
UREATES
DCU
DDMU
diuron
DMU
orbon
fenuron
monuron
neburon
PDC
THIOCYANATES
ammonium thiocyanate
potassium thiocyanate
PETROLEUM
diesel fuel
edeleanu
fuel oil
gasoline
kerosene
stoddard solvent
Non-substituted
acrolein
allyl alcohol
endothal
NPA
INORGANIC
SULFATES
ammonium sulfate
AMS
copper sulfate
ferrous ammonium sulfate
iron sulfate
sulfuric acid
CHLORATES
calcium chlorate
calcium chloride
sodium chlorate
sodium chloride
ARSENATES
arsenic pentoxide
sodium arsenite
BORATES
borax
boron trioxide
sodium borate
sodium metaborate
sodium pentaborate
sodium tetraborate
SELECTIVE
CARBAMATES
CDEC
CIPC
EPTC
IPC
SMDC
PHENOXYS
2,4-D
2,5-D
2,4,5-T
2,4-D
4-C
MCPA
sesone
silvex
TRIAZINES
amitrol
atrazine
propazine
simazin
triazine
PHENOLS
DNOC
DNOSAP
DNOSBP
SOIL FUMIGANTS
ORGANIC
calcium cyanate
calcium cyanimide
chlorpicrin
ethylene dibromide
methyl bromide
potassium cyanate
INORGANIC
carbon disulfide
ALGICIDES
copper sulfate
dichlone
quaternary ammonia
RADA
INHIBITORS
ethyl-214
maleic hydrazide
AUXILIARIES
buffers
emulsifiers
solvents
spreaders
wetting agents

WARNING

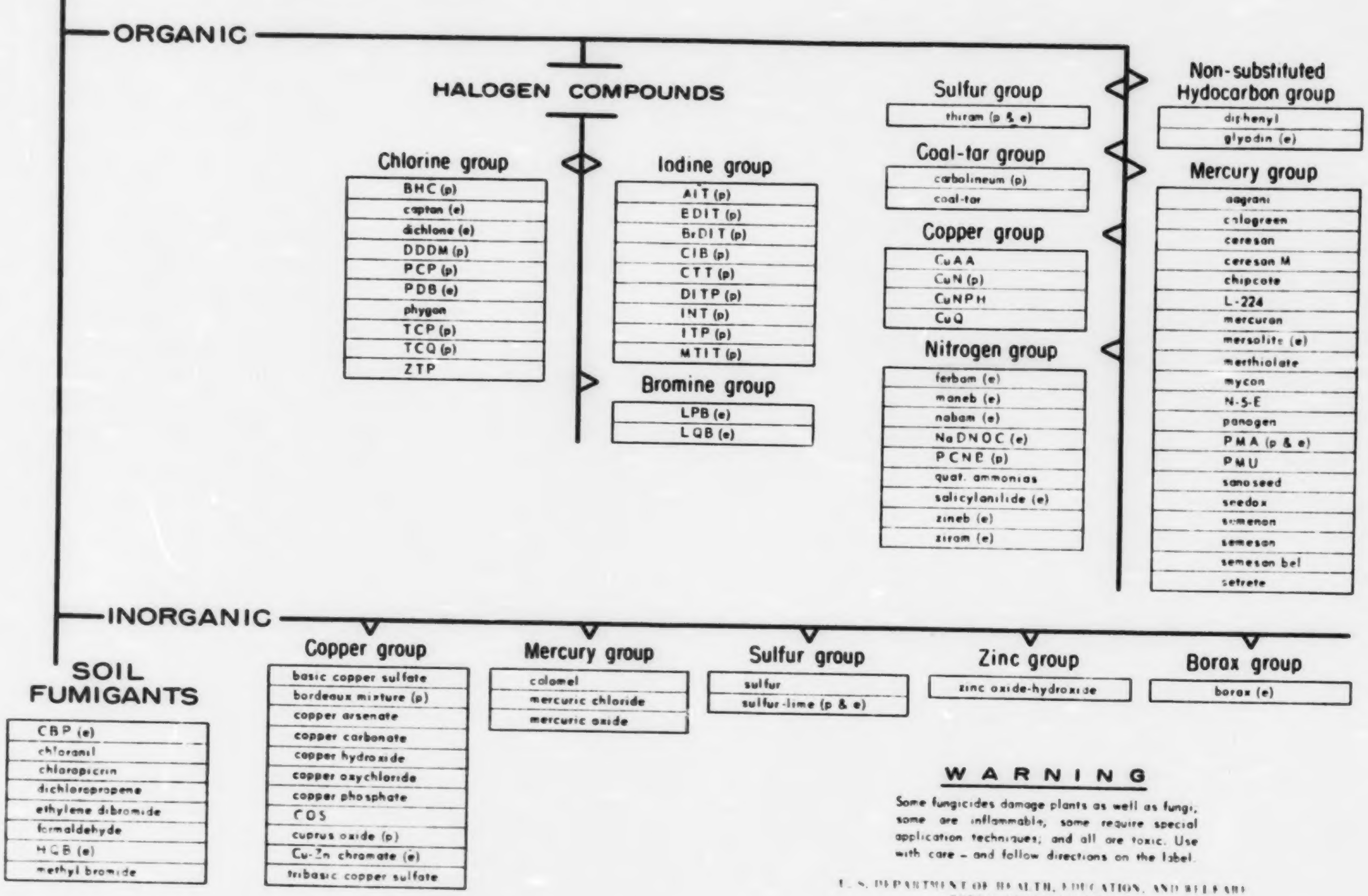
Weed control via chemicals is a useful method for abatement of mosquitoes and other animal disease vectors, however, herbicides damage useful plants as well as weeds. Some are inflammable. Some require special application techniques. All are toxic to man. Use with care, and follow directions on the label.

U. S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Communicable Disease Center
Atlanta, Georgia

HAROLD GEORGE SCOTT, Ph.D. – 1961

CHEMICAL CONTROL OF WEEDS

ECONOMIC FUNGICIDES



- ORGANIC
  - HALOGEN COMPOUNDS
    - Chlorine group
      - BHC (p)
      - captan (e)
      - dichlone (e)
      - DDDM (p)
      - PCP (p)
      - PDB (e)
      - phygon
      - TCP (p)
      - TCQ (p)
      - ZTP
    - Iodine group
      - AIT (p)
      - EDIT (p)
      - BrDIT (p)
      - CIB (p)
      - CTT (p)
      - DITP (p)
      - INT (p)
      - ITP (p)
      - MTIT (p)
    - Bromine group
      - LPB (e)
      - LQB (e)
  - Sulfur group
    - thiram (p & e)
  - Coal-tar group
    - carbolineum (p)
    - coal-tar
  - Copper group
    - CuAA
    - CuN (p)
    - CuNPH
    - CuQ
  - Nitrogen group
    - ferbam (e)
    - maneb (e)
    - nabam (e)
    - NaDNOC (e)
    - PCNB (p)
    - quat. ammonias
    - salicylanilide (e)
    - zineb (e)
    - ziram (e)
  - Non-substituted Hydocarbon group
    - diphenyl
    - glyodin (e)
  - Mercury group
    - aagrani
    - calogreen
    - ceresan
    - ceresan M
    - chipcote
    - L-224
    - mercuran
    - mersolite (e)
    - merthiolate
    - mycon
    - N-S-E
    - panogen
    - PMA (p & e)
    - PMU
    - sanoseed
    - sredox
    - semenon
    - semesan
    - semesan bel
    - setrete
- INORGANIC
  - Copper group
    - basic copper sulfate
    - bordeaux mixture (p)
    - copper arsenate
    - copper carbonate
    - copper hydroxide
    - copper oxychloride
    - copper phosphate
    - COS
    - cuprus oxide (p)
    - Cu-Zn chromate (e)
    - tribasic copper sulfate
  - Mercury group
    - calomel
    - mercuric chloride
    - mercuric oxide
  - Sulfur group
    - sulfur
    - sulfur-lime (p & e)
  - Zinc group
    - zinc oxide-hydroxide
  - Borax group
    - borax (e)
- SOIL FUMIGANTS
  - CBP (e)
  - chloranil
  - chloropicrin
  - dichloropropene
  - ethylene dibromide
  - formaldehyde
  - HCB (e)
  - methyl bromide

(p) – preventive
(e) – eradicative

WARNING

Some fungicides damage plants as well as fungi; some are inflammable, some require special application techniques; and all are toxic. Use with care – and follow directions on the label.

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
Communicable Disease Center
Training Branch
Atlanta, Georgia

WAYNE G. BROWN, 1961

SELECTION OF THE PROPER PESTICIDES FOR THE JOB

Harry D. Pratt

Pesticides are used for only one reason--to control pests, whether they are insects by the use of insecticides; rodents, by rodenticides; fungi, by fungicides; weeds, by herbicides; snails and slugs, by molluscicides; or birds, by avicides.

Therefore, in choosing the proper pesticide, some of the most important considerations are:

1. Ability to kill or control a particular pest
2. Cost
3. Safety
4. Ease of application
5. Rapidity of kill
6. Length of residual action
7. Odor
8. Staining
9. Corrosion of equipment and special precautions
10. Stages of the pest on which it will work
11. Specifity

Recently, the environmentalists have forced consideration of other factors, particularly

12. Affect of the pesticide on non-target organisms
13. Persistence in the environment

1. The ability to kill a pest may be a very simple action as with hydrogen cyanide which kills most forms of life, or a selective one as with DDT which is effective against many, but not all, arthropods. For example, it has little action on the German cockroach but controls many of the larger species such as the American and Oriental cockroaches. The development of resistant strains is forcing studies (a) to determine the level of resistance to chlorinated hydrocarbons in house flies, mosquitoes, bed bugs, body lice, fleas and many other arthropods, and (b) the best alternative insecticides, such as the organic phosphorus compounds, or carbamates[1].

2. Cost. This is a complicated consideration, not merely the price of the commercial preparation itself--but rather the cost

per gallon of the final finished spray, or of the pound of dust actually applied, or the cost per 100 or 1000 square feet of surface, or per acre, treated. The cost of three commonly used cockroach sprays will illustrate one of the most important considerations in choosing a pesticide, as shown in Table 1.

TABLE 1. COST PER GALLON OF THREE COCKROACH SPRAYS

Pesticide	Cost/Gal. Concentrate	Oz. Conc. in Final Spray	Cost/Gal. Final Spray
Chlordane (4 lb/gal)	$ 4.20	6 oz. for 2%	20¢
Diazinon (4 lb/gal)	23.00	1.25 oz. for 0.5%	23¢
Propoxur (Baygon)	14.00	8 oz. for 1%	87¢

In mosquito control today, for example, there is much discussion regarding the merits of using a few gallons of the more expensive Flit MLO or a larger quantity of the cheaper diesel oil and a surfactant. This is comparable to similar discussions as to the relative merits of killing mosquitoes by the aerial application of two quarts of a 5% insecticide per acre versus one-half pint of a 20% mixture of the same chemical, or 2 pounds of 5% granules of this pesticide. Much of this discussion which has been going on for 20 years now is being resolved by the use of the ultra-low volume (ULV) method of control, using one to three ounces of technical grade insecticide per acre. But the operator must still consider such additional factors as cost of application equipment, solvent in the case of the 5 or 20% insecticides, pay-load-carrying-ability of the spray plane, time on the ground, and acreage which can be treated in a given time. One plane with a 500 gallon tank can treat only 1000 acres per trip if the application rate is two quarts of a liquid spray per acre, whereas the same plane can treat over 20,000 acres if the application rate is 3 ounces per acre by the ULV method. The plane time on the ground, and the ability to cover enormous acreages in a short time, may be more important considerations in obtaining control after a hurricane or heavy rainfall than simple cost.

Many of the pesticides, such as pyrethrum, are expensive. Therefore synergists, materials which increase the action of the basic pesticide, are added to many formulations to increase the killing action and keep the cost within reasonable limits. An outstanding example is in the conventional household aerosol spray in which the addition of a synergist, such as piperonyl butoxide or sulfoxide, to the more expensive pyrethrum extract makes a satisfactory material which is profitable to sell or apply.

3. Safety. Some pesticides have much greater toxicity than others. Greater precautions are taken using parathion or TEPP than malathion or DDT. Most reputable companies restrict the use of cyanide to only a few highly-qualified, well-trained operators with special equipment. The very toxic rodenticide 1080 normally is sold only to companies or agencies able to certify use by trained pest control operators and to post a $50,000 surety bond. Every pesticide company, and operator, should know the type of pesticide he is using, the antidotes, and the telephone and address of the nearest Poison Control Center. Every pest control office should have a copy of the "Clinical Handbook on Economic Poisons"[2].

4. Ease of application. Some insecticides, such as malathion, can be formulated in many ways and applied as dusts, suspensions, solutions, emulsions, mists, aerosols, fogs, or as very fine particles by the ultra-low-volume method[3]. Other pesticides, such as some of the carbamates, do not go into solution easily in any of the common solvents and are formulated chiefly as wettable powders, dusts, and baits. Some of them precipitate out in cold weather, below 40°F, and form crystals which tend to clog spray nozzles. There is a growing tendency to market many of the household insecticides as aerosol sprays, for the convenience of the home-owner, even though the cost of the available pesticides may be very high in this type of formulation. Since labor is one of the most expensive items in control programs, farmers for years have combined one or more pesticides -- particularly insecticides and fungicides--into a single spray or dust to save application costs. In some cases the insecticide and fungicide have reacted chemically to produce other compounds which do not kill either insects or fungi, i.e., the sprays are incompatible. This information on compatibility of pesticides is so important that spray charts have been devised which indicate those pesticides which can be combined with no adverse reactions[4].

5. Rapidity of kill. The average housewife feels that the only "good bug" is a "dead bug". She prefers insecticides with a very rapid kill, specifically for the mosquitoes, flies, wasps, or other arthropods which annoy her. Therefore, the majority of household aerosol bombs have the vegetable insecticide, pyrethrum, as a major ingredient because it affects rapid knockdown of cold-blooded animals without harm to warm-blooded animals including man, although the final kill is usually accomplished at the present time with other insecticides such as DDT, dieldrin, malathion, carbaryl, or propoxur. In residual spraying of houses for control of mosquitoes or cockroaches the public prefers insecticides such as propoxur (Baygon) with a rapid flushing and killing action to those, such as DDT, which may take as much as an hour for the initial knockdown and a day or more for complete kill. Similarly, many pet-owners prefer carbaryl (Sevin) in a flea powder because of its rapid, pyrethrum-like action rather than the more slowly-acting DDT or dieldrin. Some of the best fly baits and wasp sprays now include dichlorvos because of its rapid action.

Because of their safety, the rodenticides most generally used by public health workers are red squill which may take a day or more to kill Norway rats once they have eaten the bait, or the anticoagulants which do not cause effective kill until the rodents have eaten the baits for four or five days consecutively or longer. There are situations, such as food-handling establishments, where the careful use of a very toxic material, such as 1080, may be justified because it kills rats and mice rapidly, usually within an hour, and without their travelling back to hiding places in walls and foundations where they might die and release a repugnant odor.

With herbicides, kerosene or mineral spirit solutions of pentachlorphenol have a rapid action (visible in less than a day) on grasses and weeds but may sterilize the ground for all types of vegetation for weeks or months. On the other hand, a 2-4-D or 2-4-5-T herbicide may take a week or more to kill, as these hormone-like materials act to make the plants literally "grow themselves to death". Both 2-4-D and 2-4-5-T sprays, however, have the advantage of killing broad-leaved weeds without killing the desirable grasses in a lawn[5].

Some avicides kill birds quickly; others have a slower action; some nauseate birds; others repel them. The fast-killing avicides are not always the most desirable long-term materials.

6. Length of residual action. Many of the chlorinated hydrocarbon insecticides, such as DDT and dieldrin, have long residual life. For many years chlordane, dieldrin, aldrin, and heptachlor have been the insecticides of choice used in termite control because a single application applied correctly as a barrier strip to the soil outside buildings, or under the slabs of homes, would provide protection for 20 years or more. Long residual action is also a desirable characteristic in sprays used to kill malarial mosquitoes, bed bugs, and cockroaches in homes, or flies in dairy barns. Many a service contract of a commercial pest control operator is based on monthly treatments of kitchens, pantries, and warehouses with residual sprays to kill cockroaches, ants, and pantry pests for periods of 30 days or longer. Careful research has indicated that there are great differences in the residual action of many of the synthetic insecticides depending on the type of surface to which they are applied. Some insecticides have a much longer life on bare or painted wood than on tile, masonite, or metal[3].

On the other hand, a short residual life is a desirable feature in many agricultural insecticides. Farmers wish to have an insecticide or fungicide which will control the pests as the fruit or vegetable are developing, yet which will not remain in toxic quantities on the fruits or vegetables when they are sold to the public. Spray schedules and the level of acceptable tolerances of many of these are listed in many official USDA and state agricultural bulletins, and other technical manuals.[6,7]

7. Odor. A number of the synthetic insecticides have characteristic odors. Benzene hexachloride (BHC) has a musty, spoiled-hay odor which is objectionable to many people, so lindane (99% gamma isomer BHC) was formulated which has only a minimal odor. The first formulations of chlordane and malathion had strong odors which have been removed by special manufacturing processes. Aldrin is preferred by some termite control companies because it is water-soluble and has little or no odor. The objectionable odor in many of the synthetic pesticides is due to sulfur impurities which can be removed in many cases by special manufacturing processes. One of the great inherent advantages of DDT is its lack of odor, particularly for residual spraying in homes or aerial applications.

8. Staining. Some pesticides, including some organic phosphorus insecticides, react with traces of lime to cause straining on sprayed surfaces. When it realized that there are traces of lime in plaster walls, whitewash, and some grades of sheetrock, it is easy to understand the magnitude and seriousness of this problem. In addition to a color staning, some solutions and emulsions may dissolve grease in dust that will stain walls or baseboards. Sprays should be very carefully applied to plastic baseboards, highly polished waxed floors, composition tile in flooring because the xylene or other solvents in some emulsions or the petroleum solvent in some solutions may cause serious discoloration or damage. Generally spraymen are given careful instructions to wipe up any excess spray with a cloth and never to allow spray run-off to remain on such surfaces. On the malaria control programs, water suspensions of insecticides such as DDT are generally used on unpainted wood or adobe type housing when the whitish residue is not objectionable, but such sprays will leave a fine, powdery deposit on painted or polished surfaces in better types of housing.

9. Corrosion of equipment and special precautions. In the 1940's when DDT residual spraying became a standard procedure in malaria control, and the synthetic insecticides such as chlordane, dieldrin, and malathion first began to be widely used, the solvents in emulsions, such as xylene, were very corrosive to natural rubber hoses and gaskets in sprayers. Manufacturers developed special neoprene types of hoses and gaskets which were much more resistant to these chemicals. Spraymen using some of the first formulations of chlordane found it necessary to clean out their sprayers and flush out their hoses at the end of each day. If sprayers were left filled over a weekend with some of the early formulations of chlordane, the chemical sometimes caused corrosion of the equipment. Later formulations are much improved. In using Dibrom,

special care must be taken of the equipment, such as flushing the chemical out of the sprayers carefully, blowing out the last traces of spray with nitrogen, using fiber glass tanks, etc. to avoid corrosion of the equipment. In using malathion, the manufacturer recommends the addition of a special sludge inhibitor, Thiosperse, to prevent the formation of deposits in the sprayers. Certain wettable powders used to make water suspensions will "set up" almost like plaster of paris if left too long in spray tanks. Therefore, users are warned to have agitation in their sprayers during spraying and to clean out their equipment carefully at the end of each day's operation.

10. Stages of the pest on which it will work. The egg and the pupa stages of most mosquitoes are more resistant than the larval or adult stages. The first stage larvae, late fourth stage larvae, and pupae of most mosquitoes do not feed and therefore cannot be controlled by particulate insecticides such as Paris green which work as stomach poisons. In the case of moths and butterflies, the caterpillar has chewing mouthparts and can be controlled by stomach poisons while the adult stage feeds on the nectar of flowers. A stomach poison applied to the leaves of plants controls the caterpillar stage very well but has no effect on the adults. Similarly, insecticides applied to lawns control soil insects, such as the white grub stage of June bugs and the Japanese beetle, without having any effect on the adults which feed on leaves, fruits, and vegetables.

11. Specificity. In many areas the use of the same insecticide for many years tends to kill out the susceptible portion of an insect population. The survivors which interbreed produce populations which show increasing resistance or cross-resistance to the insecticide or group of insecticides. Therefore, alternative insecticides must be used to control the pests. Classic examples of the use of alternative insecticides include the progressive use of

(1) Chlordane (a chlorinated hydrocarbon), diazinon (an organic phosphate, and Baygon (a carbamate) to control resistant German cockroaches.

(2) DDT, dieldrin, malathion, dimethoate, and Baygon to control resistant houseflies.

(3) DDT, dieldrin, malathion, and Baygon as residual sprays to control resistant *Anopheles*.

(4) DDT, lindane, and malathion to control resistant body lice.

The house fly and certain species of mosquitoes in some areas, such as parts of California, have been exposed to a gamut of insecticides toxicants for 25 years and are now resistant to most of the chlorinated hydrocarbons, organic phosphorus, and carbamate insecticides. Renewed attention has therefore been given to basic sanitation, new classes of insecticides, or oils in the case of mosquito control workers.

With herbicides the various 2-4-D and 2-4-5-T formulations have been widely used to control many types of broad-leaved dicotyledon plants, while an entirely different group has been recommended to control grasses and other types of monocotyledon plants[5].

12. Affect of the pesticide on non-target organisms. Many of the pesticides, particularly the chlorinated hydrocarbon insecticides, are concentrated by living organisms, particularly those in the aquatic habitat. Such materials as DDT and dieldrin have been studied in detail. Oysters, for instance, will concentrate DDT 70,000 times higher in their tissues than it occurs in surrounding water. Although DDT and dieldrin may be very effective in controlling mosquito larvae, these materials also are taken up by organisms in the food chain and appear in progressively greater quantities in such organisms as plankton, copepods, small fish, larger fish, grebes, osprey, or even the bald eagle. There is evidence that DDT may affect fish in the salmon family, such as trout and salmon; cause noticeably thinner egg shells in such birds as the brown pelican, falcon, American osprey and bald eagle. There is experimental evidence from the Patuxent Wildlife Research Center that DDE, a metabolite of DDT, reduces the bird's ability to provide calcium for egg shells, causing premature breakage. DDT sprayed on elm trees to control bark beetles carrying the spores of the Dutch elm disease fungus from diseased to healthy trees also fell to the ground beneath these trees, was concentrated in earth worms, and later caused heavy mortalities in worm-feeding birds such as robins. As a result of such research, and widespread publicity by the environmentalists and bird-lovers,

(1) The use of chlorinated hydrocarbon insecticides has been suspended as mosquito larvicides, being replaced by such materials as petroleum oils or certain organic phosphorus compouds such as Abate, or Dursban.

(2) DDT has been replaced by methoxychlor as a black fly larvicide.

(3) DDT has been replaced by methoxychlor as an insecticide to kill bark beetles in the Dutch elm disease control program[9,10].

13. Persistence in the environment. Many of the chlorinated hydrocarbon pesticides have a long life. There is evidence that materials such as DDT, chlordane, and dieldrin may remain bound up with organic material in the ground for 10 to 20 years or longer. Therefore, in mosquito control some of the organic phosphorus compounds, carbamates, and petroleum oils are not recommended as larvicides. As a result of a careful study,

the Mrak Commission recommended that these persistent chlorinated hydrocarbons should be progressively removed from general use in 1970 and 1971[9]. In March 1971, Mr. William D. Ruckelshaus, Administrator, Environmental Protection Agency deferred decision to prohibit the use of DDT and certain other pesticides pending further study.

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NONCHEMICAL METHODS OF INSECT CONTROL

Thomas J. Henneberry

The growing concern of the public and scientists concerning the demonstrated adverse effects of insecticides has stimulated renewed entomological effort to develop effective, efficient insect controls which are compatible with and have minimum effect on the complex components of the agro-ecosystem. The methods of insect control available to the entomologist today are the results of more than one-hundred years of careful observation, experimentation, and creative thinking by scientists concerned with insect control. The present era of pest control using synthetic chemicals began during World War II. The benefits to mankind attributed to the use of these chemicals for insect control is inestimable. However, problems have arisen. Adverse effects on parasites and predators, chemical residues, arthropod resistance to chemicals and high cost and temporary nature of the treatments have been of increasing concern to everyone involved in pest control.

Other methods of insect control; varietal resistance, biological agents, sterility, cultural techniques, repellents, attractants, and many other procedures have long been recognized and recommended by scientists as having potential in insect control programs. The Entomology Research Division of the USDA began to reorient its research program in 1955 from major emphasis on conventional insecticides to more selective chemical and nonchemical methods to control major insect pests (1). At the present time approximately 16% of the resources of the Division are devoted to insect control using conventional insecticides as compared to 84% in research to develop alternative methods of control and fundamental entomology studies as shown in the tabulation.

MAJOR LINES OF WORK	Percent of Resources By Group	Percent of Resources Subtotals
CONVENTIONAL INSECTICIDES	16	16
OTHER CONTROL METHODS		
Biological control	14	
Insect sterility	12	
Plant resistance	7	51
Cultural and mechanical methods	4	
Attractants, hormones, etc.	14	
FUNDAMENTAL ENTOMOLOGY		
Basic insect biology	19	
Metabolism	2	
Taxonomy	6	33
Insect transmission of plant and animal diseases	2	
Apiculture	4	
		100%

Resistant Plants

One of the most satisfactory methods of preventing damage to plants is through the development of varieties resistant to insect attack. Painter (2) broadly characterized the causes of plant resistance as follows:

1. Preference and Non-Preference

   Plants may not be acceptable to insects for oviposition, food, or shelter because of color, odor, lack of chemical or physical stimuli and/or other similar factors.

2. Antibiosis

   Plants may have an adverse effect on the biology of the insect and in some cases feeding on them may result in death.

3. Tolerance

   Plants may be tolerant to insect attack and sustain numbers that would severely impair or kill more susceptible types.

One of these mechanisms or a combination of all may make plants resistant to attack.

Outstanding achievements have been made in developing wheat varieties resistant to Hessian fly (Myetiola destructor (Say)) and wheat stem sawfly (Cephus cinctus Norton) alfalfa varieties to spotted alfalfa aphid (Therioaphis maculata (Buckton)) and corn varieties to European corn borer (Ostrinia nubilalis (Hübner)) (3), At one time the Hessian fly caused high economic losses in the United States. Today these losses are minimal largely due to the development of resistant wheat varieties. At least 23 are now available to the farmer. Similarly the dramatic discovery of a solid stem wheat variety which was resistant to wheat stem sawfly resulted in an estimated $4 million annual saving to wheat farmers.

The spotted alfalfa aphid was first discovered in New Mexico in 1954. A crash program was initiated in 1955 and in only 3 years Federal and State scientists working cooperatively developed and released the resistant variety Moapa. Subsequently, many other resistant varieties have been developed. Estimates of savings to the farmer range from $35-70 million annually.

The most destructive pest of corn in the United States is the European corn borer which caused an estimated $350 million damage in 1949 alone. A continuing program of incorporating corn borer resistance in hybrid corn has been a major factor in reducing these losses more than 60% on an annual basis.

Continuing research in all of these programs is essential since experience has taught us that insects can and do change biologically, adjusting and adapting to the types of plants grown in their environment. The identification and incorporation of multiple resistance to an insect pest is especially desirable. If the insect readily adapts to one resistance mechanism, it will probably not adapt to the other, and thus the variety will still be useful

Often, the level of insect resistance found in commercially useful varieties is not adequate to prevent economic damage by an insect pest. However, such resistance may still be useful because it can reduce the frequency of application and the amount of chemicals required to produce adequate control. This in turn reduces production cost, pollution problems, and may have a sparing effect on parasites and predators.

Research in developing plants resistant to insect attack is a challenging and new area of study. Resistance to pests exists throughout nature and needs only to be discovered, identified, and applied to solve many of our serious pest problems.

Sterility Methods

Methods of using induced sterility to control or eradicate insect populations are among the most significant recent contributions to entomology. The best known, the method of sterile insect release, involves the sustained overflooding of native populations with sterile insects of the same species at densities that are high enough so little probability exists of fertile native matings. The method was hypothesized about 1937 by Dr. Edward F. Knipling, Entomology Research Division, U.S. Department of Agriculture. Then after many years of research, it became scientific fact when screw-worm flies, Cochliomyia hominivorax (Coquerel), sterilized by irradiation with cobalt-60, were released at the rate of 800 per square mile on Curacao Island in the Netherlands Antilles in 1954. Eradication was complete about 3 months after the first release (4). Subsequent releases of sterile screw-worms in Florida (The Southeast Screw-Worm Eradication Program) and in the Southwest were similarly successful (5, 6). Expenditures in the Southeast screw-worm sterile-release program were less than 10 million dollars, and the estimated savings to cattle growers in that area since its conclusion probably exceed 100 million dollars. In the Southwest program, the investment is about 20 million dollars, but livestock men estimate savings of as much as 400 million dollars.

A second method, chemical sterilization of insects, is now being investigated. Chemicals that have sterilizing effects on insects have been known for many years. However, interest in their potential in insect control programs was renewed when the screw-worm eradication campaigns were successful and La Brecque (7) found 3 alkylating agents that induced sterility in both sexes of house flies, Musca domestica (L.). If effective methods of using these sterilants can be developed, it is possible that they can be used both to sterilize insects for mass releases and also to sterilize a native population.

The Method of Sterile Insect Release

Suppression of insect populations by the method of sterile insect release requires the mass rearing of the subject species, the inducing of sterility, and the sustained release of the sterile insects into the wild population in such numbers that the probability of a fertile native mating becomes progressively more remote as the releases continue. This constant pressure on reproductive potential results in a marked decrease in and theoretical elimination of the insect population within a relatively few generations.

For example, Knipling's (8) calculations indicate that when 90% of the total insect population in the first generation consists of released sterile insects and the same number of sterile insects are released each subsequent generation, the native population will be eliminated by the fourth generation. In contrast, a program of control with insecticides which kills 90% of the insects in each generation would theoretically require more than 10 generations to eliminate the population. The initial effect of both systems is the same, but the sustained release of sterile insects each succeeding generation has a progressively greater effect on the reproductive potential of the native population; applications of insecticides produce a constant pressure each generation and therefore require more than 2.5 times as long to produce the same total effect.

The essential prerequisites that must be satisfied for the elimination of a particular insect include an efficient method of mass rearing, techniques of sterilization that have no adverse effects on the mating capability, competitiveness, or vigor of the species, a practical and efficient means of disseminating the sterile insects into the native environment, and assurance that the released insects will not create undue hazards or loss to crops, livestock, or man (8).

Another essential prerequisite is that the initial releases of sterile insects must produce high enough overflooding ratios of sterile to native insects to start a downward trend in the population. Information about the distribution of the native population and quantitative and qualitative information about the population density, particularly at the low cycle of the population, is therefore essential. Sterile insect releases are highly efficient when the population is small; conventional insecticides are least efficient against small populations and highly efficient when populations are large. Thus, the optimum time to begin a program of sterile insect releases is when the active native population is at its lowest level, and the proper timing for all releases must be critically and exactly determined.

Also, a sterile insect release program will be effective only when the reproductive potential of the total population or of a large segment of it is suppressed. Since many insect species are capable of moving great distances, the full effect of the technique can probably only be fully demonstrated on isolated populations unless the migration of native insects into the experimental areas can be greatly reduced or prevented.

Sterilizing Native Populations

If chemical sterilants could be used to sterilize insects in a native population, the expense of mass rearing and releases would be eliminated and the sterilized insects would remain in the population to compete sexually with unsterilized native insects. This latter effect would be a bonus and would further reduce the reproductive potential of the native population. For example, if an insecticide kills 90 of 100 insects of each sex in a population, 10 pairs will remain to mate and produce the next generation. If a sterilizing agent renders 90 of 100 insects of each sex in a population incapable of reproduction, the 10 males that avoided the sterilant compete in mating for the 10 remaining females with the 90 sterilized males. We would expect only 1 fertile mating to result from this combination. Moreover, the sterilized population would compete in time and space in the insects' ecosystem (9). The use of chemosterilants with various baits and attractants appears a promising method of inducing sterility in native insect populations.

Knipling and McGuire (10) developed seven hypothetical population models to evaluate the potential of sex attractants in insect control programs. Essentially, their findings indicated that: (a) a trapping or appropriate system of treatment in which the ratio of the equivalents of the competing sex attractant (synthetic, extract, or caged virgin females) to the number of wild females in the population was high would greatly reduce the probability of native male matings; (b) the total impact of the system of treatment on the reproductive potential of the population would not be affected by the number of matings attempted by males but would increase if females were attracted to male attractants and attempted multiple matings before oviposition; (c) killing the attracted males would be only slightly less effective than sterilizing them; and (d) the most efficient system of sterilizing a native population would be realized if both sexes were attracted and sterilized. The authors also indicated that releases of sterile males combined with the use of baited chemicals (sex attractants) that would kill or sterilize the native males would substantially increase the degree of population control. In addition, they showed that theoretically the use of a given number of caged virgin female insects as sex attractants would be as effective as the release of the same number of sterile males; also, they would achieve the same increasing degree of effectiveness as the native population declined as would releases of sterile insects.

The theoretical considerations are challenging, and the tremendous potential of integrated methods of inducing sterility deserve extensive consideration by researchers to evaluate their merit.

Sterility methods have been shown to have a high degree of potential for many economic insect species. For example, the potential of the method was demonstrated with the codling moth, *Carpocapsa pomonella* (L.), in limited field trials (11, 12). In a test in 1966, chemically sterilized codling moth males were released by the USDA Entomology Research Division in a 15-acre apple orchard at Yakima, Washington. The results were promising and the control obtained was as good as that obtained in orchards treated with the regular schedule of insecticidal sprays. In addition, the absence of the sprays permitted the natural predators and parasites to provide effective control of the European red mite, *Panonychus ulmi* (Koch), and the wooly apple aphid, *Eriosoma lanigerum* (Hausmann). Similar results were obtained with releases of irradiated codling moths in Canada in 1966 and at Yakima in 1967 in a 93-acre apple orchard (Butt, personal communication).

Before area-wide population control of the codling moth by the method of sterile insect release can be proved feasible and practical, a large-scale pilot program involving several thousand or more acres must be conducted. Such a project would bridge the gap between exploratory research and practical application.

The development of techniques of controlling insect populations by the method of sterile insect releases over large areas is a tremendous undertaking. The talents of many scientific disciplines are involved, and the most detailed and exacting information concerning rearing, biology, ecology, behavior, and population dynamics of the subject species is required. However, when the procedure is successfully developed and implemented, it can substantially reduce insect losses and the costs of control and can avoid the introduction of damaging side effects into our environment.

Biological Control

Biological control agents are the most important factors in regulating natural populations of noxious insects. More than 1,100 viruses, bacteria, fungi, protozoa, rickettsia, and nematodes attack insects in their environment (13). Viruses attack eighteen or more important crop pests such as the corn earworm, Heliothis zea (Boddie), the cabbage looper, Trichoplusia ni (Hübner), the tobacco budworm, H. virescens (F.), and the armyworm, Pseudaletia unipuncta (Haworth).

Spectacular results were obtained when viruses were used to control certain forest insect pests (14), and a bacterial pathogen, Bacillus popilliae Dutky, that attacks Japanese beetles, Popillia japonica Newman, provides good control of this insect (15) when it is applied as a spore dust to turf. Another bacterium, Bacillus thuringiensis var. thuringiensis Berliner, is pathogenic to about 110 species of Lepidoptera and 8 species of Diptera (16) and is recommended for control of cabbage loopers, alfalfa caterpillars, Colias eurytheme Boisduval, and the tobacco hornworm, Manduca sexta (L.)

A number of formulations or varieties of Bacillus thuringiensis have been tested for insect control. A strain has been found which, under laboratory conditions, is about 100 times more effective than strains commercially available against the bollworm on cotton and against other insect pests (17). The effectiveness of this new strain, referred to as HD-1, must be determined under field conditions before its practical value can be appraised. However, field studies to date are most promising. Other field studies have shown that a polyhedrosis virus for control of cabbage looper is just as effective and economical as insecticides. Another polyhedrosis virus has sometimes afforded the same high degree of control of the cotton bollworm. Variations in test results with insect viruses are believed to be due to the way in which they have been formulated, and efforts are being made by industry to develop improved and more stable formulations. Like chemical pesticides, much toxicological data will be required to prove the safety of an insect virus before it will be registered and receive approval for use.

Control of agricultural pests by parasites and predators has also had some marked successes (18). One aspect of the use of insect parasites and predators for insect control involves exploration, introduction, evaluation, distribution, and establishment so that they will become a part of the environment and contribute to the control of destructive insect pests. Another aspect is to protect native beneficial insects which play a very important role in regulating destructive pest populations. Attempts have been made to introduce parasites and predators of about 80 pests into the U.S. over a span of more than 80 years (19, 20). Of about 520 species that have been imported, 115 have become established, but only about 20 have provided important control of some of our worst pests. Introductions of beneficial insects have proved quite useful against several scale insects, the European corn borer, gypsy moth (*Porthetria dispar* (L.)), alfalfa weevil (*Hypera postica* (Gyllenhal)), Rhodes-grass scale (*Antonina graminis* (Maskell)), and others. One approach that deserves considerable attention is the possibility of mass rearing insect parasites and predators for sustained release to supplement the native forms in the environment.

The possibility is now being investigated in the Blue Mountain area of Washington where large acreages of canning peas are grown and pea aphids, *Acyrthosiphon pisum* (Harris), are a problem. The pests overwinter on alfalfa plants that are also reservoirs of pea enation and pea streak viruses, and then the alate aphid forms migrate to peas in the spring (21). About 100 million braconid parasites, *Aphidius pulcher* Baker and *Aphidius smithi* Sharma and Subba Rao, were therefore reared and released in the spring of 1966 to determine the effectiveness of these parasites in controlling the populations of pea aphids developing on the alfalfa. Also, portable polyethylene-covered greenhouses were developed and placed over dormant alfalfa in the winter to protect the plants from the weather and to force growth four to six weeks ahead of the alfalfa in the surrounding fields.

These field nurseries were then stocked with laboratory-reared pea aphids and parasites. As the populations of parasites in the cages developed, they were allowed to escape through temperature-controlled automatic roof vents (22). The results to date indicate that substantial control of pea aphids on alfalfa was obtained with subsequent reduction in migrations to pea plantings. The possibility of controlling pea aphids by this method appears promising.

Field tests have shown that two mass releases totaling 292,000 predatory aphid lion, *Crysopa carnea* Stephens, eggs or larvae per acre was as effective against the bollworm on cotton as the best available insecticides (23).

Attractants

Insects respond positively to many chemical, biological and physical stimuli. Entomologists have visualized the potential of manipulating the resulting behavioral responses to achieve economic control of pests through trapping and killing, luring and sterilizing, or disrupting their mating behavior.

The most potent and specific insect attractants appear at present to be the sex pheromones, and Jacobson (24) recently compiled a list showing that such pheromones have been demonstrated in more than 200 insect species.

At present, we have completed the isolation, identification, and synthesizing of the sex pheromone of only a relatively few insects. One of the most recent was that of the cabbage looper (25). However, while the chemists were still working to produce the synthetic pheromone, researchers were using living female moths to investigate possible ways of using the attractant when it was ready.

One of the first approaches was to combine living virgin female moths and a trap equipped with a blacklight lamp which is known to attract and catch cabbage looper moths. When the two attractants were combined to produce a baited trap, more male insects were captured in the baited traps than in traps equipped with either blacklight or virgin females alone (26). Thus when the breakthrough in synthesis came, investigators were ready to evaluate the potential of the synthetic pheromone in the field (27).

A ranch near Red Rock, Arizona, that includes 3,110 acres, 2,240 acres of which are in crops, was selected for the test. (Annually about 1,000 acres are planted to fall lettuce, 800 acres to spring lettuce, and 200 acres to cotton.) The installation of blacklight traps baited with synthetic cabbage looper sex pheromone at the rate of about one trap unit per six acres of cultivated ground was completed in March 1966. To date, collections of female cabbage looper moths in a check area about nine miles away have been 14 times greater and catches of male cabbage loopers have been 30 times greater than in the control lighted area. Also, though egg and larval counts have varied considerably, fewer eggs and larvae were found on lettuce in the trapping area compared with the check area. Thus, the results appear promising though the intensive use of insecticides on the ranch makes it impossible to evaluate the full impact of the baited traps.

Since 1966 research has been conducted on the island of St. Croix, U.S. Virgin Islands to evaluate the effects of traps equipped with blacklight lamps on populations of the tobacco hornworm. The approximately 3 traps per square mile installed on the 84-square-mile island became operational in June 1967. However, for about 1 year before the lights were turned on, 9 separate traps were operated to develop baseline information on the magnitude and seasonal distribution of the populations. Also, in 1968, after Hoffman et al. (28) demonstrated that baiting light traps with virgin female hornworm moths resulted in marked increases in the catch of males, all the light traps on the island have been baited with virgin female moths.

Since the traps began operating, the populations of tobacco hornworm moths have decreased consistently; in March 1968, they appeared to be about 30-40% as high as the populations recorded before the experiment. Also, after the traps were baited with virgin female moths in March 1968, the male catches increased about 6-10 times in the baited traps compared with the catch in unbaited traps. Moreover, for about 6-8 weeks after the first baiting of the light traps, 4-5% of the females collected in the traps were unmated. This percentage increased to about 6-10% for several months to a peak of 30% virgin females and declined thereafter to a relatively constant rate of 14-16% unmated females. Another indication of the effect of baited traps on populations of male hornworms is the decrease in the percentage of males caught in unbaited traps from a fairly constant 60% before the baiting to about 40% at the present time. Thus, the population of tobacco hornworms on the island of St. Croix measured by catches in the light traps now appears to be about 20% of that present on the island before the beginning of the experiments (W. Cantelo and J. Smith, personal communication). The results are in the preliminary stages of evaluation, but we hope they will provide us with some answers about how light traps can fit into programs for control of hornworms.

The possible use of sex pheromones in preventing orientation or through mating inhibition is also an exciting new concept.

One phenomena that has been observed by investigators studying male behavior after stimulation to sex pheromones is adaptation or attenuation of response after prior conditioning stimulus. The threshold concentration of pheromone necessary to induce response is raised for a time following the period of exposure. Cabbage looper males may not respond to a given threshold concentration for several hours after first exposure to the pheromone (29, 30).

Many investigators have proposed that if high enough concentrations of pheromone were maintained over large areas, native females could not contribute enough additional pheromone to result in orientation to them and males would never locate females to inseminate them. Under field conditions a concentration of 1×10^{-10} g/liter completely prevented orientation of males to pheromone-emitting females (31).

The potential of an attractant combined with a toxicant to provide low-cost control of a pest over a large area was demonstrated when the oriental fruit fly, Dacus dorsalis Herdel, was eradicated on the island of Rota (32). Methyl eugenol, a powerful male attractant, was combined with 1% naled and impregnated in cane-fiber squares. The squares were dropped from aircraft flight lines about five miles apart, except for inhabited areas where bait stations were used. Daily monitoring with traps showed an immediate 93% reduction in fly populations. After 10 drops, no flies were captured and none have been found during the 24 subsequent months of trapping and inspecting of host fruits. Only 3.5 grams of toxicant/acre were required for the entire program.

Repellent Techniques

Although great progress in insect control has been made with insecticides, these killing agents do not prevent viruliferous insects from infecting crop plants; such vectors must be killed almost instantly or prevented from feeding.

Numerous investigators have observed and reported on the response of aphids to color and light (33, 34, 35). Also, the repellent effect of aluminum foil on insects was first observed in 1949 by Lester Wall, Reynolds Metal Co., Richmond, Virginia (unpublished report), and Kring (36) reported that when unpainted aluminum pans were placed around yellow pan traps, aphids avoided the yellow pan traps. Smith (37) therefore began tests in 1963 at Beltsville, Maryland to determine whether this phenomena could be used to repel flying aphids and reduce incidence of viral infections in crops.

In one test in 1965, 50% of the soil area of each field plot of bush squash at Beltsville, Maryland was covered with sheet aluminum foil. Other plots were untreated or sprayed with an effective aphicide. The presence of the aluminum sheets reduced the catch of aphids by more than 95% compared with the catch in unmulched check plots and in plots sprayed with an insecticide during a 3-day period of heavy aphid flight. Also, the number of infected plants in the mulched plots was greatly reduced for 6 to 7 weeks compared with virus infected plants in the sprayed and untreated plots, and the yields of squash in the mulched plots were 6 times greater (38).

In another test at Long Island, New York, mulches of reflective aluminum and also of white plastic reduced catches of winged aphids in yellow pan traps by more than 87% and decreased the spread of cucumber mosaic virus in gladiolus plantings (39). Other researchers who have used such a mulch have reported reduction of lettuce mosaic in lettuce plots (40) and protection of roses from flower thrips, Frankliniella tritici (Fitch), injury (41). Aluminum mulches have not been effective with all aphids on all crops (42, 43); however reflective mulches with plastic or paper backing can be produced to a wide range of specifications, and growers of some commercial crops are trying such mulches to warm the soil early and to achieve control of weeds and aphids.

Insect Hormones

Another recent trend is research on insect hormones and hormonelike materials that disrupt insect development rather than to cause immediate death. Sterility in adult insects may result soon after treatment with molting hormones or their analogs, whereas juvenile hormones act by interrupting insect development and in some cases produce monster insects that finally die or, should they attain adulthood, cannot reproduce because of their physical abnormalities (44). Some of these hormonal materials, which would not be expected to have a detrimental effect on nontarget organisms, are effective against test insects at small dosage rates, about 1 nanogram or one-billionth of a gram. New "hybrid" synthetic ethers, which are juvenile-hormonelike materials, have been found to block normal insect growth and development. These compounds, some of which are fairly easy to synthesize, often show greater potency than the insects' own hormones or biologically similar synthetic compounds previously tested (45).

Cultural Techniques

In the Pacific Northwest, the green peach aphid is also the most important vector of beet western yellows and beet yellows viruses, diseases that cause annual losses of as much as 25 to 30% of the yield of sugarbeets (46). Also, unfortunately, beet western yellows, the most prevalent of the yellows diseases there, can be harbored by 30 or more hosts other than beets and, therefore, serve as reservoirs of the virus (47). As noted, the green peach aphid overwinters primarily in the egg stage on peach trees in the general area, but small numbers of the summer forms overwinter and feed on plants growing year-round in protected places, and intensive ecological studies made between 1962 and 1964 showed that many of these overwintering hosts of the summer aphid forms were also alternate hosts of beet western yellows virus (48, 49). Also, warm spring-fed drainage ditches in sugarbeet-growing areas near Toppenish, Washington proved to provide a micro-climate 20-50°F. warmer than the surrounding environment where the weeds and aphids could fluorish throughout the year. Thus, though aphids from eggs overwintered on peach trees are free of virus until they feed on diseased plants, the summer aphid forms that overwinter on infected weeds carry the virus to young sugarbeet plants when they migrate to them in the spring.

These findings stimulated studies to determine whether eliminating overwintering populations of aphids and weed hosts from drainage ditches would reduce viral infections in nearby sugarbeet fields. A 22- and a 30-square-mile area southwest of Toppenish, Washington that contained 42 to 53 miles of drainage ditches was the test area; a similar area 4 miles east of the experimental area served as a check. During January, February, and March 1965-1967, before sugarbeets began growing and aphids began migrating, the weeds in the drainage ditches in the test area were destroyed by burning. In 1966, 91% fewer aphids and 76% fewer diseased plants were found in the area where the ditches were burned than in the unburned check areas; in 1967, 75% fewer diseased plants were found in the burned area than in the unburned check area. The increased yield in the test area was estimated at more than 2 tons per acre, and the cost of ditch burning per acre of sugarbeets protected ranged from $2.20 to $6.85 and averaged $4.00 for the three years. This cost compares favorably with the average estimated cost of $16.00 per acre for conventional chemical sprays.

The results of this research have been received enthusiastically by the sugarbeet-growing industry and the individual growers in the area, and they have now contracted to have the ditch burning done on a routine basis as part of their regular process of insect control.

Another example of the method of host elimination or replacement to reduce an insect population concerns the beet leafhopper, Circulifer tenellus (Baker), in Idaho. This insect is the sole known vector of curly top virus in the United States, and the large desert and range areas in southern Idaho where weed-host plants (several species of broad-leafed annual plants) have become established and serve as overwintering and spring hosts. (Russian thistle is the most important summer host). Scientists recognized that the breeding areas proper might be the vulnerable link in the host-plant cycle and postulated that if it were broken, effective control of the insect could be obtained. (The acreage of Russian thistle is smaller than that of annual weed hosts and appeared more vulnerable to control.)

The Bureau of Land Management, Department of the Interior therefore began seeding the summer breeding areas of the beet leafhopper in Idaho in 1959 with crested wheatgrass, Agropyron cristatum (L.) Gaertn. The cost per acre of this seeding ranges from $3.25 to $6.00 per acre depending on the method used. Also, the Plant Pest Control and Entomology Research Divisions, Agricultural Research Service, U.S. Department of Agriculture, and the Idaho Bean Commission have cooperated in advisory capacities. Since the program began, permanent crested wheatgrass has been seeded over more than

200,000 acres of range (50, 51).

Before the seeding program began, curly top virus caused losses in sugarbeet yields of as much as 65%. Also, the beet leafhopper transmitted the virus to beans, tomatoes, and other agriculturally important crops. Since the initiation of the program, the situation has changed remarkably. Curly top has been reduced to a minor problem, and the establishment of crested wheatgrass has increased the carrying capacity of range for annual grazing ten-fold, in addition to increasing the dependability of available range forage and reducing the hazards of grass fires and wind erosion (51, W. Peay, personal communication). Thus, the outcome is a fine demonstration of an effective, economical, and efficient method of controlling an insect through the application of many scientific disciplines to the solution of a common problem.

Integrated Control

Integrated control is a system designed to use all available, suitable, and necessary methods of controlling insects to reduce pest populations and maintain them at levels below economic thresholds. The development of integrated control systems are based on exacting and definitive information on the biology, ecology and population dynamics of the pest species in the complex agro-ecosystem being considered. Although literally hundreds of insects may occur, there are usually 1 or 2 major insect pests which cause economic damage. These are the key species which must be controlled with minimum or no effects on the other complex components of the ecosystem and their interactions. Picket and McPhee were among the first to recognize the adverse effects of the unilateral chemical approach to ordered pest control and they developed valid principles for an integrated control program which has provided guidelines and influenced the direction of subsequent research.

The majority of entomologists recognize the mistakes of the past. Recognizing the variety of methods of insect control now available it is imperative that all consideration be given to developing logical, effective and efficient systems through combinations of these methods. Thus, we can bring maximum pressure on pest insect populations while minimizing the impact on the entire agro-ecosystem.

Summary

Research designed to develop and exploit alternative nonchemical methods of insect control demand the most exacting and sophisticated information on insect biology, behavior, movement, ecology, and population dynamics. The focus of research must be directed at an entire key insect population or a large segment of it since these methods are designed to suppress or reduce the insect population to a level below its economic threshold. Many insect species are capable of moving great distances and methods designed to reduce such populations in local or very limited areas have a low probability of success because insects migrating from great distances often prevent successful reductions of the total population in the management area.

In recent years there have been a number of significant successes in the application of nonchemical methods for insect control. However, no one method appears to be adequate to solve all insect problems or even, in many cases, the same insect problem under different ecological conditions. In many cases, there may not be a single method which will accomplish effective control but a combination of methods which are logically and effectively integrated may be required to bring maximum pressure on an insect population.

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THE DIAGNOSIS AND TREATMENT OF ACUTE PESTICIDE INTOXICATION IN MAN

G. A. Reich

Pesticide poisoning is reported by the National Clearinghouse for Poison Control Centers at about 5,000-6,000, cases per year. This represents, for the most part, accidental poisoning among children. Many more cases than this occur, especially among pesticide exposed workers, but there are few reports of these. The fatality rate in pesticide poisoning is considerably higher than that seen with the more common agents in poisoning such as aspirin, tranquilizers, and birth control pills.

The incidence of pesticide poisoning varies a great deal from region to region in the U.S.A., being highest in agricultural areas and in urban centers surrounded by agricultural areas.

Poisoning at times occurs on a mass scale when flour, sugar, or the like, become contaminated with pesticides in transit or in storage, since pesticides survive the cooking and baking processes quite well. Examples of these are the food poisoning episodes of recent years in the Middle East, Columbia, and Mexico. Episodes on a much smaller scale have occurred in the U.S.A.

The Community Studies have been conducting prospective epidemiological studies of workers exposed to pesticides to determine if their health is being adversely affected. In addition to this, our Studies provide diagnostic and therapeutic assistance in their local areas to Doctors handling cases of acute poisoning. Most of our reports to date have come from south Texas and south Florida which represent primarily cases of individual poisoning but at times are of group poisoning.

In south Texas, the incidence of poisoning increased for several years, then declined only to rise again. Most cases occurred in June and July during the period of greatest pesticide use. Most cases were among teen-agers and young adults who were employed by farmers and spray pilots to assist in mixing and applying pesticides. Parathion and methyl parathion were the usual agents, and the route of exposure was almost always dermal. Very few deaths occurred, even though pesticides are by far and away the leading cause of poisoning in this area.

The signs and symptoms observed in these cases indicate that a variety of biochemical and physiological functions are altered by pesticides. The central nervous system, cardiovascular system, gastrointestinal system, and musculoskeletal system are the most obviously affected in pesticide poisoning. The diagnosis may be difficult, because of this variety of signs and symptoms which are suggestive of other conditions as well as pesticide poisoning.

In south Florida, poisoning reflects three sorts of circumstances: (1) accidental ingestion by 1 to 2 year old children in and around the house; (2) accidental dermal exposure in occupational exposed workers; and (3) suicidal ingestion in middle-aged to older adults. Numerous pesticides have caused deaths in this area, ranging from old types like Paris Green up to newer pesticides like Zectran. In Florida, pesticide poisoning is a year round phenomenon rather than coinciding with the season of greatest agricultural use of pesticides. This is due to the importance of the accidental cases among children and the suicidal cases among adults. The highest death rates are among adults, but this represents the fact that such a large proportion of these are suicidal. The agents of most importance are the organophosphates, especially parathion, but numerous compounds singly or in combination have been involved. There have been several homicidal attempts with pesticides too, most of which have been successful. In this area, the leading cause of death from poisoning among children is pesticides.

How important pesticide poisoning is in your area will depend upon several factors already noted. Determining what the true incidence is in any particular area may be difficult, because of errors in diagnosis and the lack of an effective system of reporting. Such poisoning is, however, preventable -- though suicidal cases present particular problems.

When one considers that only about 10% of the true incidence of poisoning in the U.S.A. is reported, and that the Poison Control Centers report over 100,000 cases per year, it is apparent that poisoning (not just with pesticides) represents an important public health problem.

CHRONIC BIOLOGIC HAZARDS DUE TO CHEMICAL POLLUTANTS WITH ILLUSTRATIVE REFERENCE TO PESTICIDES

Samuel S. Epstein, M.D.

A. Introduction

The benefits and hazards of technology are escalating at unprecedented paces. The benefits of technological achievement, especially those related to specific products, can usually be translated into early and often predictable economic gains; any errors in such predictions economically penalize a very small segment of the population. Hazards--consumer, occupational and environmental--associated with technological achievement are usually unpredictable, necessitate extensive evaluation, once suspected, and hence are generally viewed as impediments by the innovator. It has long been recognized as unrealistic to expect industry to voluntarily devote the time and resources for safety evaluation commensurate with what is required. Thus, legislative and regulatory mechanisms have been gradually evolved to improve product safety and to minimize harm to humans and to the environment. The validity and utility of these mechanisms is now being critically examined.

Concern for environmental quality, consumer, and occupational safety is burgeoning, and some classic assumptions of industrial society are under challenge. Apparent conflicts have developed between the needs for continued economic growth and for environmental management. The degree of polarization on these issues is reflected in divergent current attitudes to recent restrictions on such products as DDT, and cyclamates. It is thus timely to review some basic problems of chemical pollution, develop methods for anticipating and detecting human and environmental hazards, and consider alternative or supplementary legislative and regulatory mechanisms for more rational and effective management.

B. COMPARTMENTS OF THE ENVIRONMENT

The chemical environment consists of three primary compartments--air, water, and soil--which co-exist in a state of dynamic equilibrium. Although a particular pollutant may be initially distributed predominantly in one primary compartment, generalized translocation may ensue, especially for persistent pollutants or for pollutants that yield persistent degradation products. Food--a secondary compartment--reflects possible contributions from pollutants in air, water and soil.

C. CATEGORIES OF CHEMICAL POLLUTANTS

Although the term pollutant is often perjoratively restricted to synthetic industrial chemicals, there is a wide range of other important chemical pollutants; these fit into four broad categories. The first group consists of natural chemicals in excess, and includes nitrates which are normal dietary components. At high concentrations in food or water, nitrates can cause acute methemoglobinemia in infants. The possible occurrence of chronic subclinical methemoglobinemia in infants following intake of moderately elevated nitrate levels in water has been recently reported (Gruener and Shuval, 1969; Epstein, 1970d). Also, nitrates as reduction products of nitrates, may interact in vitro or in vivo with secondary amince to form nitrosamines, some of them carcinogenic, teratogenic, and mutagenic in microgram doses (Lijinsky and Epstein, 1970). Oxides of nitrogen--a major class of atmospheric pollutants--can also interact with secondary amines to yield nitrosamines.

Natural fungal or plant toxins in crops comprize the second group of chemical pollutants, of which aflatoxins and cycasins are notable examples. The yields of these toxins can generally be considerably influenced by technological factors, such as conditions of harvesting, storage, and processing (Goldblatt, 1969).

The third group consists of complex organic and inorganic mixtures, such as air and water pollutants, which comprize a wide range of undefined as well as partially defined components.

Finally, there is the group of synthetic chemicals--agricultural chemicals, notably pesticides and fertilizers; food additives, which may be intentional, such as antioxidants and dyes, or accidental, such as pesticides, heavy metals, and plasticizers; fuel additives; household chemicals; industrial chemicals, and in a somewhat specialized class, therapeutic and prophylactic drugs, and drugs, and drugs of abuse.

D. CATEGORIES OF ADVERSE HUMAN EFFECTS DUE TO CHEMICAL POLLUTANTS

Pollutants may induce a wide range of adverse biological effects in man, which are generically and collectively termed toxicity. Acute or chronic toxicity per se may be expressed in fetal, neonatal, perinatal, childhood or adult life, in effects ranging from impairment of health and fitness to mortality. More specific manifestations of chronic toxicity include carcinogenecity, teratogenicity, and mutagenicity. The possibility that chronic toxicity is also manifest in immunological impairment or in psycho-behavioral disorders has yet to be explored.

Some pollutants may induce one or more of these types of toxicity. Pollutants or their chemical precursors may also interact in vitro and in vivo to produce otherwise unanticipated synergistic toxicity. Synergistic effects can also result from interactions between particular pollutants and otherwise harmless and common environmental chemicals.

E. MATCHING BENEFITS AGAINST HAZARDS

The need to use many synthetic industrial chemicals makes it essential to recognize and estimate the human and environmental hazards they pose and their acceptability with regard to the matching benefits they confer. The costs of one malformed child, based on remedial and custodial care alone and excluding deprivation of earnings, have been recently estimated as about $250,000 (Oberle, 1969). Such costing is clearly impossible for genetic hazards, the scope of whose effects in future generations cannot be predicted. Externalized environmental costs have till recently been ignored or discounted.

Hazards from a particular synthetic chemical need not necessarily be accepted even when matching benefits appear high, as equally efficacious but non-hazardous alternatives are usually available. The mandatory criterion of efficacy, once extended from therapeutic drugs to other synthetic chemicals, such as food additives and pesticides, may well simplify such equations, especially for hazards from synthetic chemicals with no demonstrable benefits for the general population.

F. CAUSE FOR CONCERN

There is now little doubt that many diseases hitherto regarded as spontaneous, including cancer, birth defects, and mutations, are caused by environmental pollutants. This realization is heightened by the exponential increase in human exposure to new synthetic chemicals--and their degradation and pyrolytic products in air, water, and soil--which, in general, are inadequately characterized toxicologically and environmentally.

1. Carcinogenicity as a Public Health Hazard:

Recognition is now growing that the majority of human cancers are probably due to chemical carcinogens in the environment, and that they are hence ultimately preventable; there is also growing interest in the role of chemical carcinogens in activating tumor-producing viruses. Epidemiological studies have revealed wide geographical variations in the incidence of cancer of various organs in the general population; in some instances these studies have incriminated local environmental pollutants.

The pandemic incidence of lung cancer in the U.S.A., and even more so in the U.K, has been casually and clearly associated with tobacco smoking; a contributory role for air pollution also seems likely. The high incidence of cancer of the oral cavity in Asia, representing some 35 per cent of all Asiatic cancers in contrast to one per cent of all European cancers, is clearly related to the chewing of betel nuts and tobacco leaves. The high incidences of liver cancer in the Bantu and in Guam are probably due to dietary contamination with aflatoxin, a potent fungal carcinogen, and to eating of Cycad plants, containing azoxglucoside carcinogens, respectively. The high incidence of gastric cancer in Japan, Iceland, and Chile has been associated with high dietary intake of fish; suggestions have been made implicating nitrosamines, formed by reactions between secondary amines in fish and nitrite preservatives. The high incidence of cancer of the esophagus in Zambians drinking Kachasu spirits may be related to its high nitrosamine contamination. More restrictedly, a wide range of occupationally-induced cancers are well recognized. These include bladder cancer in the aniline dye and rubber industry; lung cancer in uranium miners of Colorado and in workers in nitrogen mustard factories in Japan; nasal sinus cancer in wood workers; pleural and peritoneal mesotheliomas in asbestos workers; and skin cancer in cutting and shale oil workers.

Two major classes of environmental carcinogens may be identified. First, potent carcinogens, such as aflatoxins and nitrosamines, which can produce cancer in experimental animals, even at the very low levels in which they have been found in foods. Identification of these carcinogens in foods has encouraged attempts to link their distribution with local patterns of cancer incidence. Second, weak carcinogens, such as atmospheric pollutants. certain pesticides and food additives, whose effects may easily escape detection by conventional biological tests. Additionally, as such weak carcinogens are unlikely to be clearly implicated epidemiologically, they may pose as great hazards as more obvious potent carcinogens. In spite of these difficulties, there is considerable epidemiologic support for a causal relationship between community air pollution and lung cancer. There are marked regional differences in lung cancer mortality patterns in the U.S.A.; increased mortality is clearly related to increased urbanization and to increased levels of organic pollutants in the air. The higher lung cancer rates in urban areas cannot be fully explained by factors such as smoking or occupation. In a survey some 12 years ago, lung cancer rates in the U.S.A., standardized for smoking besides age, were found to be 39/100,000 in rural areas and 52/100,000 in cities with populations in excess of 50,000 (Hammond and Horn, 1958); similar surveys in England also confirmed the importance of this urban factor, and stressed its interaction with smoking (Stocks, 1969). This urban excess, of 25 per cent in U.S.A. mortality, is generally regarded as being due to air pollution. Confirmatory evidence is also afforded by several studies on immigrants who tend to retain the incidence pattern of lung cancer of their country of origin, even through they assume the smoking and other habits of their country of adoption.

2. Mutagenicity as a Public Health Hazard:

The first evidence that environmental pollutants may influence the genetic constitution of future populations resulted some four decades ago from the discovery that high energy radiation induces mutations. The subsequent development of nuclear energy added a new dimension and enhanced awareness to the problem of genetic hazards. Safeguards have been accordingly developed to minimize radiation exposure. Once radiation-induced mutagenesis was discovered, there were reasons to suspect that some chemicals would act similarly, but proof of this was delayed until World War II, when mustard gas was shown to induce mutations in fruit flies. Many and varied types of chemicals have subsequently been shown to be mutagenic. The likelihood that some highly mutagenic chemicals may come into wide use, or indeed may already be in wide use, is now causing serious concern.

A mutation is defined as any inherited change in the genetic material. This may be a chemical transformation of an individual gene, which is designated a gene or point mutation, that causes it to have an altered function. Alternatively, the change may involve a rearrangement, or a gain or loss, of parts of a chromosome, which may be microscopically visible, and which is designated a chromosome aberration. In many systems, these are easily distinguished, but in human studies, classification of an individual defect, whether due to a point mutation or a chromosome aberration, is not always possible.

Mutations may occur in any somatic or germ cell. The result is frequently the death of the particular cell involved, and generally, this causes only local and transient damage. However, if the genetic functioning of the cell is altered, while the capacity for cell division is unimpaired, the mutation may be transmitted to descendant cells. These effects may result in cancer or birth defects in somatic cells of the adult or fetus, respectively. Mutations in germ cells are more serious still, as these may be transmitted to future generations. It should be emphasized that there is no single type of mutagenic effect. Since every part of the body and every metabolic process is influenced by genetic control, the range of effects produced by gene alterations includes all conceivable types of structure and process. At one extreme are consequences so severe, so-called lethal effects, that the individual cannot survive. If cell death occurs very early in embryonic development, it may never be detected; extensive cell death at a later stage, may lead to abortions. Approximately one-fourth of spontaneous abortions shows a detectable chromosome aberration; there is no way at present to know how many of the remainder are caused by gene mutations or by visually undetectable chromosome aberrations. If the embryo survives until birth, a variety of physical abnormalities may manifest. There are numerous known inherited diseases, and probably many more that are unknown, all of which owe their ultimate cause to mutations. While these are individually rare, collectively, they are a cause for serious public health concern. At the other extreme are gene mutations with mild effects. Finally, those with still smaller effects may be imperceptible. In between these extremes are the whole gamut of genetic defects.

Mutations can produce a wide diversity of deleterious effects. Many mutations produce effects similar to those produced by other, non-genetic causes. The impact of environmental mutagens is thus statistical rather than unique. This problem is further complicated by the time distribution of mutational effects. Some mutant genes are dominant, in which case, the abnormality or disease will appear in the immediate generation following occurrence of the mutation. Dominant mutations express themselves as early fetal deaths, or in abnormalities, such as achondroplasia, polydactyly, retinoblastoma, and sterility. On the other hand, the mutation may be recessive, requiring the presence of abnormal genes in both homologous chromosomes--one derived from each parent--to produce the effect. Recessive mutations, such as albinism, Fanconi anemia, amaurotic idiocy, and phenylketonuria, may then be unexpressed for many generations. The major effects of increased mutation rates would thus be less obvious and spread over many generations, and would include ill-defined abnormalities, such as premature aging, and enhanced susceptibility to various diseases, notably leukemia and cancer, and alterations in sex ratios (Crow, 1968; Report of the Advisory Panel on Mutagenicity, HEW, 1969).

The great majority of mutations are harmful or at best, neutral. This has been established experimentally and is a deduction from the principle of natural selection (Crow, 1968). Natural selection has previously eliminated those individuals whose mutant genes caused them to be abnormal. As a result, an approximate equilibrium has been established between the introduction of new mutant genes into the population and the elimination of old mutant genes by natural selection. With present high standards of living and health care, many mutants that in the past would have caused death or reduced fertility now persist. The equilibrium is thus out of balance, and new mutants are being added to the population faster than they can be eliminated. Thus, coupled with the near eradication of many infectious diseases, makes it likely that future medical problems will be of increasingly genetic origin. As Lederberg has recently stated (Lederberg, 1971), "If we give proper weight to the genetic component of many common diseases which have a more complex etiology than the textbook examples of Mendelian defects, we can calculate that at least 25 per cent of our health burden is of genetic origin. This figure is a very conservative estimate in view of the genetic component of such griefs as schizophrenia, diabetes, atherosclerosis, mental retardation, early senility, and many congenital malformations. In fact, the genetic factor in disease is bound to increase to an even larger proportion, for as we deal with infectious disease and other environmental insults, the genetic legacy of the species will compete only with traumatic accidents as the major factor in health."

A mutation, once it has occurred, may be transmitted to succeeding generations. If the gene causes a lethal or sterilizing effect, it will persist only one generation and affect only one person. On the other hand, if it causes only slight impairment of health, it may be transmitted from generation to generation. There is, therefore, generally an inverse relation between the severity of the gene effect and the number of persons that will be exposed to this effect. The effects of mild mutants could otherwise be dismissed as relatively unimportant. But in any overall consideration, many persons mildly affected may be considered as of comparable importance to one individual severely affected. Experiments on Drosophila show that mildly deleterious mutations occur with much greater frequency than more severe mutants. Thus, although an increased mutation rate would cause a corresponding increase in severe abnormalities and genetic diseases, the major statistical impact of a mutational increase would be to add to the burden of mild mutation effects, which would be of major public health consequence and yet difficult to detect.

Chemical mutagens in the environment pose hazards which have not yet been quantitated, although sensitive and practical mammalian test systems are available. A report of the genetic study section of the National Institutes of Health states (Crow, 1968): "There is reason to fear that some chemicals may constitute as important a risk as radiation, possibly a more serious one. Although knowledge of chemical mutagenesis in man is much less certain than that of radiation, a number of chemicals--some with widespread use--are known to induce genetic damage in some organisms. To consider only radiation hazards is to ignore what may be the submerged part of the iceberg."

The report further states: "Recent investigations have revealed chemical compounds that are highly mutagenic in experimental organisms, in concentrations that are not toxic and that have no overt effect on fertility..."

Ethyleneimines are good examples of highly mutagenic chemicals which are used for many purposes, including therapy of neoplastic and non-neoplastic diseases, chemosterilant insecticides, pigment dyeing and printing, fireproofing, and creaseproofing of fabrics and textiles, ingredients in solid rocket fuels, intermediates in many industrial syntheses, and as cross linking agents in starches and shampoos. A joint USDA-Dow chemical study is currently determining whether ethyleneimine-modified flours and starches can be used as paper sizing agents. Ethyleneimines have also been proposed for rodent and plant control. Another example of a mutagen in common use is trimethylphosphate, which till recently was added to gasoline at concentrations of 0.25 g/gallon for controlling surface ignition and spark plug fouling. It is also used as methylating agent, chemical intermediate in production of polymethyl polyphosphates, flame-retardant solvent for paints and polymers, and catalyst in preparation of polymers and resins. Trimethlphosphate is mutagenic in the dominant lethal assay in mice, and produces chromosomal damage in bone marrow cells of rats following oral or parenteral administration at subtoxic doses (Epstein, 1970a; Adler, Ramaro, and Epstein, 1971). It is, however, difficult to estimate mutagenic hazards to which the general population has been exposed in the absence of information on the concentration of unreacted trimethylphosphate and of biologically active pyrolysis products in automobile exhaust. Similar considerations apply to recent fuel additive formulations based on triarylphosphates.

Fortunately, recent recognition of genetic hazards due to chemicals has been paralleled by the development of various tests for mutagenicity (Report of the Advisory Panel on Mutagenicity, HEW, 1969). Sub-mammalian test organisms--bacteria, Neurospora, yeasts, plants and Drosophila--help elucidate basic mechanisms. But in view of the wide metabolic and biochemical discrepancies between these systems and man, sub-mammalian tests should be used to provide data ancillary to more relevant test systems. Of these, three *in vivo* mammalian tests are practical and sensitive--*in vivo* cytogenetics, the host-mediated assay, and the dominant lethal assay; results from these latter tests can be extrapolated to man with some confidence (Report of the Advisory Panel on Mutagenicity, HEW, 1969).

3. Teratogenicity as a Public Health Hazard:

Teratology is the study of congenital malformations. These are generally defined as structural abnormalities which can be recognized at or shortly after birth, and which can cause disability or death. Less restrictedly, teratology, also includes microscopical, biochemical, and functional abnormalities of prenatal origin. The incidence of human congenital malformations is unknown in the absence of a comprehensive National registry; it has been variously and minimally estimated as ranging from 3-4% of total live births. Three major categories of human teratogens have so far been identified: viral infections, X-irradiation, and chemicals, such as mercurials, and thalidomide. Although the teratogenicity of various chemicals has been experimentally recognized for several decades, only after the thalidomide disaster of 1962 were legislative requirements for three-generation repofductive tests established; the appropriateness of these as tests for teratogenicity has been questioned (Report of the Advisory Panel on Teratogenicity, HEW, 1969).

G. METHODS FOR PREDICTIVE TESTING AND MONITORING OF ADVERSE HUMAN EFFECTS

1. Toxicity Testing:

Pollutants to which man is exposed must be tested for acute and chronic toxicity per se, and also for the more specific effects of carcinogenicity, teratogenicity, and mutagenicity. Historically, each of these effects has been studied and applied independently and by non-converging disciplines. Toxicity per se has largely been the province of classical pharmacologists, generally with little interest in carcinogenesis or mutagenesis. This apparent parachialism was exemplified by the commonly held view in the mid-fifties that the chronic toxicity test is inappropriate for determining carcinogenicity (Barnes and Denz, 1954); the belated regulatory requirement for teratogenicity evaluation--imposed somewhat indirectly, however, as a 3-generation reproductive test--in response to the thalidomide disaster, is further illustrative. Mutagenesis has been even more isolated than other aspects of toxicology. Indeed, publications on mutagenic hazards are still rarities in toxicological or public health journals and, in general, appear only in genetic journals. The present fragmentation of toxicological research thus appears somewhat artificial. New organizational patterns and training programs are needed to co-ordinate toxicological approaches, and to make toxicology more responsive to current needs.

New and more sophisticated methods for toxicity testing, which are more sensitive and responsive to low and even ambient levels of individual chemical pollutants and various mixtures of pollutants, reflecting more realistic patterns of environmental exposure, must be developed. Illustrative, is the recent demonstration (Paulson and Dubos, 1971), that a wide range of non-specific stresses, including temporary deprivation of food, cage crowding, parturition, and lactation, markedly increased the toxicity of ambient levels of DDT to rodents.

2. Test Agents:

Toxicity testing must not be confined to the test agent per se, but should extend to its chemical and metabolic derivatives, its pyrolytic and degradation products, and its contaminants and reaction products. These considerations are further accentuated when the various derivatives or degradation products are of toxicological or environmental consequence. Illustrative, are the presence of polychlorophenol contaminants and their dioxin pyrolytic products in phenoxy herbicides (Epstein, 1970b), cyclohexylamine as a contaminant and human metabolic product of cyclamates (National Academy Sciences, National Research Council, Report, 1968), and the uncharacterized biodegradation products of the detergent nitrilotriacetic acid (Epstein, 1970d, 1970e). It is thus obvious that comprehensive safety testing demands availability of detailed chemical and comparative metabolic data on the agent under test. The requirements for such data may necessitate carefully controlled metabolic studies in human volunteers, once safety has been established in comprehensive animal tests.

In any form of toxicity testing, agents must be administered acutely, subacutely, and chronically to reflect the role of hepatic microsomal enzyme function in activation and detoxification. It may also be necessary, in particular circumstances, to test for effects of concomitantly administered and otherwise non-toxic chemicals, that may induce or inhibit microsomal enzyme function. Experiments must be designed to reflect the role of possible interactions between test agents--administered by any route--and between dietary factors and other chemicals, such as accidental and intentional food additives, drugs, and air pollutants.

3. Route of Testing:

Routes of test administration inter alia should reflect human exposure. While inhalation is the obvious route for testing of air pollutants, the importance of this route for other pollutants has been generally underestimated. Respiratory exposure is of particular human significance for pesticide aerosols and vapors. Surprisingly, there are no data in the pesticide literature on chronic inhalation tests. While useful information may also be derived from tests involving inappropriate routes of administration, extrapolation from these data to human experience should be cautious. However, to demonstrate weak carcinogens in the environment, it is essential that the most sensitive available test system be used, and that the factor of comparability of route of administration be subordinated to the requirement of sensitivity. Once an effect has been clearly established, the quantitative relevance of the experimental data to the human situation should be considered before limits can be reasonably proposed; only at this stage does it become appropriate to weight factors, such as route of administration. To use such factors in a limiting sense, and to insist on precise comparability between test systems and human exposure before the problem of hazard is established, may effectively limit the possibility of detecting weak environmental carcinogens; such limitations would also challenge the human implications of all but the most recent data on experimental tobacco carcinogenesis.

4. Test Species:

Ideally and minimally, two mammalizn species should be tested for toxicity per se, carcinogenicity, mutagenicity, and teratogenicity. In certain circumstances, when there is specific information that the rodent metabolism of the chemical pollutant in question is qualitatively different from that in humans, other more appropriate species, such as pigs, and sub-human primates, may also be tested. Reliance on small numbers of pigs or primates is no substitute for conventional rodent tests and may even mislead. Special considerations, may dictate the use of less common species in particular circumstances.

5. Dosage and Insensitivity of Animal Test Systems:

For carcinogenicity, teratogenicity, and mutagenicity, pollutants must be tested at higher levels than those of general human exposure (Reports of the Advisory Panels on Carcinogenicity, Mutagenicity, and Teratogenicity, HEW, 1969); irrespective of route of administration, maximally tolerated doses are recommended for this purpose as the highest dose in dose-response studies. Testing at high doses is essential to the attempt to reduce the gross insensitivity imposed on animal tests by the small size of samples routinely tested, such as 50 or so rats or mice per dose level per chemical, compared with the millions of humans at presumptive risk (Reports of the Advisory Panels on Carcinogenicity, Mutagenicity, and Teratogenicity, HEW, 1969). To illustrate, assume that man is as sensitive to a particular carcinogen or teratogen as the rat or mouse; assume further that this particular agent will produce cancer or teratogenic effects in 1/10,000 humans exposed. Then the chances of detecting this in groups of 50 rats or mice, tested at ambient human exposure levels, would be very low.

Indeed, samples of 10,000 rats or mice would be required to yield one cancer or teratogenic event, over and above any spontaneous occurrences; for significance, perhaps 30,000 rodents would be needed (Epstein, et al., 1969). Of course, in any particular instance, humans may be less or more sensitive than rodents to the chemical in question; there is consequently no valid basis for the prediction of the relative sensitivities of test animals and man. Thus, meclizine, an antihistamine drug used in treatment of morning sickness, is teratogenic in the rat, but not apparently in the few women studied (King, 1965; Yerushalamy and Milkovich, 1965). Contrastingly, for thalidomide the lowest effective human teratogenic dose is 0.5 mg/kg/day; the corresponding values for the mouse, rat, dog and hamster are 30, 50, 100, and 350 mg/kg/day, respectively (Kalter, 1968). Thus, humans are 60 times more sensitive than mice, 100 times more sensitive than mice, 100 times more sensitive than rats, 200 times more sensitive than dogs, and 700 times more sensitive than hamsters. Similar considerations obtain for certain aromatic amines, such as 2-naphthylamine, which are potent bladder carcinogens for man and dogs, but not for rats, mice, guinea pigs, and rabbits (Hueper, 1969). Hence, to predict a safe level for thalidomide or for 2-naphthylamine, from rodent data or from derived mathematical models, would expose humans to grossly unwarranted hazards.

Apart from the gross insensitivity of animal test systems, and the impossibility of gauging human sensitivity from animal tests, ample data on interactions between carcinogens further confirm that it is not possible to predict safe levels of carcinogens based on an arbitrary fraction of the lowest effective animal dose in a particular experimental situation. As HEW Secretary Flemming stated ten years ago (Flemming, 1960): "Scientifically, there is no way to determine a safe level for a substance known to produce cancer in animals". Thus, the production of hepatomas in trout by feeding as little as 0.4 parts per billion of aflatoxin B_1 is sharply enhanced by addition of various noncarcinogenic oils to the diet (Sinhuber et al., 1968). Similarly, carcinogenesis for mous skin of low concentrations of benzo [a]pyrene and benz[a]anthracene is increased 1000-fold by the use of the noncarcinogenic n-dodecane as a solvent (Bingham and Falk, 1969). Intratracheal instillation of benzo[a]pyrene and ferric oxide in adult hamsters elicited a high incidence of lower respiratory tract tumors only in animals pretreated at birth with a single low dose of diethylnitrosamine (Montesano, Saffiotti, and Shubik, 1970). Such considerations underlie the 1958 Delaney Amendment to the Federal Food, Drug and Cosmetic Act, which imposes zero tolerances for carcinogenic food additives. The amendment states"...no additive shall be deemed to be safe if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal...". Zero tolerances should also be imposed for occupational carcinogens, such as asbestos.

It must also be emphasized that testing at high dosages does not produce false positive carcinogenic results. There is no basis whatsoever for the contention that all chemicals are carcinogenic or mutagenic at high doses. To illustrate, in the recent Bionetics study, sponsored by the National Cancer Institute, about 140 pesticides were tested orally in mice of both sexes and strains at maximally tolerated doses from the first week of life until sacrifice at 18 months; less than 10% of these pesticides were found to be carcinogenic (Report of the Advisory Panel on Carcinogenicity, HEW, 1969; Innes et al., 1969).

Experimental finding of carcinogenicity, mutagenicity, and teratogenicity in synthetic industrial chemicals, such as pesticides and food additives, is unusual. Once carcinogenicity has been determined, similarly efficacious but noncarcinogenic alternatives are generally available. Methoxychlor, for instance, can replace the persistent and carcinogenic DDT; moreover, the efficacy of DDT for its major usage in the U.S.A.--cotton insect control--is now questionable due to the emergence of insecticide resistance (Environment, 1969; Bosch, 1970). Similar considerations obtain for Mirex, another persistent and carcinogenic insecticide, whose utility for the eradication of the imported fire ant, which is at worst a minor pest, has been recently challenged (Coon and Fleet, 1970). These considerations apply with even greater emphasis to carcinogenic intention food additives, such as the recently banned cyclamates, that were virtually useless for the general population (Epstein, et al., 1969).

Special pleadings, reflecting narrow economic and social interests, for the continued use of carcinogenic chemicals--albeit at reduced levels based on arbitrarily derived supposed safety margins--are unacceptable.

6. Monitoring and Epidemiological Surveillance:

Persistent chemicals, chemical, and metabolic derivatives of less persistent chemicals, and their reaction and pyrolytic products, should be detected and monitored in the environment--air, water, soil, and food--and in body fluids or tissues of plants, animals, and man. Selectively, only those chemicals or degradation products with known or presumed toxicological relevance should be monitored.

Even with well-planned and well-executed toxicologic testing, it is likely that unexpected adverse effects from pollutants will be seen in man, reflecting the insensitivity or inappropriateness of the test systems. Epidemiological surveys of human and animal populations may provide post hoc information on geographical or temporal clusters of unusual types or frequencies of adverse effects--including cancer, birth defects, and mutations--after exposure to undetected or untested pollutants in the environment. Such surveys are complicated by the long interval which may elapse between exposure and subsequent adverse effects. This may be measured in decades for cancer and in generations for mutations.

Epidemiologic techniques serve to detect trends or fluctuations in mortality, morbidity or disease patterns. Provided that clear differentials in exposure levels to pollutants exist in the general population, epidemiology may then correlate particular toxic effects with particular pollutants; the relationship between heavy cigarette smoking and lung cancer is a classic example of such a relationship. However, these relationships are more difficult to establish when exposure differentials are minimal, as with a food additive consumed by the general population at not widely dissimilar levels. Additionally, logistic considerations, quite apart from inadequate current surveillance systems, may limit the utility of epidemiological approaches even when temporal or geographical clusters of adverse effects have developed. Disquietingly, no major known human teratogen--X-rays, German measles, mercury, or thalidomide--has been epidemiologically identified, even in industrialized countries with good medical facilities (Report of the Advisory Panel on Teratogenicity, HEW, 1969).

One of the most critical needs is the development of comprehensive National surveillance and registration systems for birth defects and for mutations. This could simply operate by referral of any obvious birth defects to a specialized regional center. As the incidence of obvious birth defects in the U.S.A. is approximately 2 per cent, this sample would be likely to include effects induced by environmental teratogens or mutagens. Recognition of temporal or geographical clustering of such effects might permit the isolation of causal environmental influences.

To be of value in monitoring mutation rates, special indicator traits must be selected. These would have to be dominant, unique, present obviously and conspicuously at virth, and be associated with sterility, to obviate the possibility of parental transmission. In addition to such relatively gross approaches, more refined monitoring procedures could be developed cytogenetically and biochemically, both as intrauterine and neonatal tests.

The use of spontaneous abortions has been recently recommended as a simple and practical method for monitoring mutation rates (Bateman, 1970). The required parameters would include the proportion of pregnancies spontaneously aborting; the proportion of abortions due to fetal failure rather than maternal malfunction; the proportion of analyzable abortuses with chromosome aberrations; and the incidence of chromosome aberrations, such as trisomy, XO, and polyploidy. The most informative single statistic for monitoring the mutation rate would be the proportion of all pregnancies with an XO abortus; the spontaneous incidence of these is approximately one per cent. The same data could be used to monitor for polyploidy, nondisjunction--parallel increase of both trisomy and XO--and for teratogenic effects--which would also be detected amongst full-term pregnancies. Teratogens may also produce chromosome aberrations, but as they act after fertilization, the aberrations will b sporadic against a normal background. The action of teratogens would therefore be recognized by an increase in abortions with a basically normal karyotype.

Apart from testing of first generation progeny, the feasibility of monitoring peripheral blood cells for cytogenetic aberrations and for protein changes--resulting from altered gene function--may give more immediate measures of enhanced mutational rates.

High risk occupational groups have in the past provided important epidemiologic data on hazards to the general public, such as carbon monoxide, aromatic amines, dioxins, nitrosamines, asbestos, enzyme detergents, and heavy metals. It is to be hoped that adequate legislation will be developed and enforced to exclude or sharply curtail the continued use of workmen as unwitting guinea-pigs for society. In this connection, it should be pointed out that available National Consensus Standards relate to only a small fraction of toxic chemicals to which workmen are exposed, and further that most of these standards are based on grossly inadequate and out-of-date information.

7. Insensitivity of Current Toxicological and Epidemiological Techniques:

Current toxicological techniques are insensitive and relatively limited in their ability to detect weak carcinogens, and other toxic agents, individually and in various combinations or mixtures realistically reflecting low or ambient levels and patterns of environmental exposure. Similarly, epidemiological techniques are unlikely to detect weak carcinogens and other toxic agents, unless there are sharp differentials in exposure of the general population, as with the cigarette smoking. For widely dispersed agents, such as intentional or accidental food additives, to which the population at large is generally exposed, human experience is unlikely to provide any meaningful indication of safety or hazard.

H. ILLUSTRATIVE CURRENT PROBLEMS WITH PESTICIDES

1. Persistent Chlorinated Hydrocarbons:

Persistent chlorinated hydrocarbon pesticides are characterized by their extreme stability and persistence, their lipid solubility, and their biological magnification and accumulation in food chain. Persistent and carcinogenic pesticides include Aldrin, Dieldrin, Endrin, Chlordane, Heptachlor, DDT (including DDD and DDE) and Mirex (Innes, et al., 1969; Report of the Advisory Panel on Carcinogenicity, Report of the Secretary's Commission on Pesticides and their Relationship to Environmental Health, 1969). The use of such pesticides on food crops, leading to ingestion of their residues in food, is in clear violation of the Delaney Amendment to the Food, Drug and Cosmetic Act of 1958 which states that "no additive shall be deemed safe if it is found to induce cancer when ingested by man or animals". Proper implementation of the Delaney Amendment demands the immediate and absolute ban on the production and distribution of such persistent carcinogenic pesticides. As Secretary Flemming stated (1968),--"The Amendment is based on the simple fact that no one knows now to set a safe tolerance for substances in human foods, when these substances are known to cause cancer when added to the diet of animals".

a. DDT:

Over the last 20 years DDT has been shown to be carcinogenic in various strains of mice and rats, and also in fish. These findings have been clearly confirmed in a recent study sponsored by the National Cancer Institute (Innes, et al., 1969). In this definitive study, approximately 130 pesticides were fed to male and female mice of two strains at maximally tolerated doses from the seventh day of life until sacrifice, approximately 18 months later. Apart from negative controls, positive controls, using six generally accepted carcinogens of varying potency were also used. DDT at a daily dosage of 46.4 mg/kg, equivalent ot 140 ppm, produced a high incidence of hepatomas and malignant lymphomas. The relative risk for the development of tumors in mice fed with DDT was shown to be approximately four times that of the negative controls and between one-third and one-half that of the positive controls. These data on the carcinogenicity of DDT in a wide range of animal strains and species unequivocally demonstrate its highly significant potential carcinogenic hazard to man.

DDT has been shown to be mutagenic in rats in the dominant lethal assay, at doses from 80-200 mg/kg, administered orally or parenterally (Legator, 1970). Recent studies have also demonstrated that non-toxic dietary levels of DDT, comparable to ambient levels of human exposure, greatly increase the sensitivity of rats to the toxic effects of a wide variety of non-specific stresses such as cage-crowding, parturition, lactation, and partial starvation (Paulson and Dubos, 1971). Additionally, ecological hazards induced by DDT, including effects on phytoplankton, and reproductive failure in a wide range of carnivorous birds are now well recognized.

The major use of DDT in the U.S.A. is for cotton crop pests; such applications are of problematic efficacy as most cotton insect pests are already DDT-resistant (Environment 1969; Bosch, 1970). Additionally, effective non-persistent and non-carcinogenic alternatives, such as methoxychlor are currently available.

b. Mirex:

Mirex is carcinogenic in mice (Innes, et al., 1969); at daily doses of 10 mg/kg, equivalent to 26 ppm, it produced a high incidence of hepatomas in two strains of mice. The development of tumors in Mirex-fed mice was nearly five times that of the negative controls and about one-half that of the positive controls. In view of such considerations, currently proposed extensive programs for the wide scale use of Mirex for the eradication of the Imported Fire Ant appears unjustifiable. Furthermore, there are no available data which indicate that the Imported Fire Ant represents an economic or human hazard; at worst, the ant can only be regarded as a minor pest, comparable to bees and wasps (Coon and Fleet, 1970).

2. PHENOXY HERBICIDES:

2,4,5-T and various of its esters were shown to be teratogenic in three strains of mice and in rats (Report of the Advisory Panel on Teratogenicity, Report of the Secretary's Commission on Pesticides and their Relationship to Environmental Health, 1969); 2,4-D and some esters were also teratogenic. These data cannot be discounted by the claim that the sample of 2,4,5-T tested was contaminated with relatively high concentrations of dioxins, as four recent studies with purified 2,4,5-T have confirmed its teratogenicity (Epstein, 1970b, 1970c). The continued use of phenoxy herbicides, including 2,4,5-T and its esters, on food crops and for aerial and broadcast applications clearly pose unacceptable human teratogenic hazards; such use has been prohibited in the Commonwealth of Massachusetts as from 4/28/71.

3 METHYLENEDIOXPHENYL PYRETHRIN SYNERGISTS

Various methylenedioxyphenyl compounds, particularly piperonyl butoxide (PiB.) are used to synergize the effects of pyrethrin insecticides; PiB.

is not insecticidal itself, but it inhibits enzymatic detoxification systems in insects. PiB. also inhibits detoxifying enzyme systems in mammals and man and thus may increase human susceptibility to the otherwise non-toxic effects of a variety of environmental pollutants and drugs (Epstein, 1971). The need for intensified research in this area stems from the likelihood of increased usage of PiB.- pyrethrin combinations to replace persistent and carcinogenic chlorinated hydrocarbon pesticides. These considerations were recently emphasized (Report of the Advisory Panel on Interactions, Peport of the Secretary's Commission on Pesticides and their Relationship to Environmental Health, 1969). ..."At sufficiently high levels insecticide synergists inhibit the metabolism of insecticides. Information is needed; a) as to the human intake of these synergists, both by consumption of food in the normal diet and by inhalation exposure to aerosols normally used; b) on the interaction resulting from intake of this magnitude, first with experimental animals and subsequently with man".

It must be emphasized that, unlike the situation with persistent chlorinated hydrocarbons and with phenoxy herbicides, there are no unequivocal data indicating potential human hazards from the present use of pesticide synergists. There are, however, problems which should be resolved, particularly prior to the projected expanded use of these synergists.

I. REGULATORY AND LEGISLATIVE DEFICIENCIES

1. Regulatory Deficiencies:

Federal regulatory agencies suffer from certain limitations and constraints. Jurisdiction over products and their applications are commonly fragmented among the 60 or so Executive agencies concerned with environmental problems. Additionally, there are certain categories of products, notably industrial chemicals, for which there are no or minimal regulatory controls.

Agencies are generally inadequately funded and are subjected to political pressure and lobbying by vested interests. Federal agencies tend to be preoccupied with highly visible, immediate problems as they move from crisis to crisis. Anticipation and prevention of crisis situations, which should be major aims of regulatory agencies, and the need for a more systematic approach to consumer, occupational, and environmental safety is often lacking.

2. Legislative Deficiencies:

Legislative responsibility in environmental and related areas now extends to some 20 Congressional committees. Occupational exposure to toxic chemicals and dusts, and to noise and stress, exposure of the public-at-large to industrial effluents in air and water - such as sulfur dioxide and mercury - and consumer exposure to common industrial products--such as detergents and fuel additives--are inadequately legislated, and thus inadequately regulated. DefInciencies in establishing safety criteria and deficiencies in regulatory practice may be illustrated by reference to recent or current problems: the carcinogenicity, mutagenicity, and ecological effects of the insecticide DDT; the teratogenicity of the herbicide, 2,4,5-T and its dioxin contaminants;

the carcinogenicity and mutagenicity of the food additive cyclamate; and the poorly characterized toxicology of the detergent builder nitrilotriacetic acid, quite apart from its questionable efficacy in the stated objective of preventing eutrophication due to the use of phosphate detergents. It should be pointed out that serious questions as to the efficacy and safety of nitrilotriacetic acid were only just recently raised (Epstein, 1970d, 1970e), in spite of assurances to the contrary, based on ten years industrial research. Such questions should have been raised at an earlier stage, and not after some detergent manufacturers developed irreversible and major economic committments.

J. REGULATORY AND LEGISLATIVE NEEDS

1. Enforcement of Existing Regulations and Legislation:

Approximately 600 food additives, some of which have never been adequately evaluated toxicologically are now on the FDA Generally Recognized as Safe (GRAS) list; both their toxicological and legal status is suspect. A proper enforcement of the Food Additive Amendment of 1958 would have probably precluded the majority of these chemicals from inclusion on the GRAS list. Prior to 1958, the criteria for inclusion on the GRAS list were safety, based on scientific evaluation or an experience from common usage in food; after 1958, scientific evaluation should have been the only allowable criterion. Apart from these GRAS additives, it appears that manufacturers have reserved to themselves the right to determine whether or not a food chemical is safe without informing FDA, let alone filing petitions for use. As a result, it is possible that some chemicals are being currently illegally used in food, and with no independent scientific review as to their safety.

The financial onus for safety evaluation of food additives has been placed on the manufacturer by law. Therefore, it would appear unreasonable for the tax payer to assume financial responsibility for the testing of profitable food chemicals, alleged to be Generally Recognized as Safe, as the FDA currently proposes to do.

Current enforcement of the requirement to stop feeding cattle with the carcinogenic diethylstilbestrol (DES) 48 hours prior to slaughter, so that no residues will be left in the carcass, now appears to depend largely on the voluntary cooperation of the farmers and feed lot operators. There is evidence that this requirement is not being enforced (Wellford, 1971); additionally, it appears that USDA analytic techniques for DES residues in meat are insensitive, and that the number of carcasses sampled is adequate. This problem merits urgent investigation to determine the extent of the exposure of the public to this carcinogenic food additive, and the degree to which the Delaney amendment is being violated.

Another area where Federal meat regulations are not being enforced by the USDA relates to the use of nitrite as a preservative for sliced meat products without the requirement for labelling (Wellford, 1971).

2. Criteria and Standards to be Met Prior to Use, Registration, and Introduction of Chemical Innovations Into Commerce:

Before a new synthetic chemical may be distributed into commerce and the environment, questions as to its efficacy, identity, and safety must be posed and satisfactorily answered. Similar questions should also be asked about many existing chemical pollutants, such as the GRAS food additives; these questions should additionally apply to those chemicals for which new alternatives are proposed. Questions on safety must also be resolved prior to occupational exposure to synthetic chemicals. Does the chemical in question serve a socially and economically useful purpose for the general population? If not, why introduce it and accept potential hazards without general matching benefits? Such considerations clearly apply to the use of monosodium glutamate in baby foods, and cyclamates for the public at large. The self-evident need for efficacy, now generally accepted for drugs, should be extended to all synthetic chemicals. These concepts were emphasized at a recent White House conference on nutrition, where it was recommended that food additives be excluded from products unless they either significantly improve the quality or nutritive value of the food or lower its cost as well as being safe (Kendall, 1969).

Questions on safety must be particularly rigorous for persistent chemicals--or for chemicals which yield persistent degradation products--which are environmentally mobile and lipophilic and which consequently are thus likely to accumulate in the food chain. In particular, the industrial use of such chemicals belonging to this category, such as mercury and polychlorinated biphenyls, should only be permitted under carefully controlled conditions and using closed systems in which environmental contamination is prevented and almost complete chemical recovery and recycling ensured.

Synthetic chemicals, their concentrations and impurities should be clearly labelled and identified in fuel, foods, pesticides, household, and all other formulations. Arbitrary exemption of particular products from labelling requirements creates unfortunate precedents, and unpredictable toxicological situations.

Besides clear identification of the chemical in question, information about its chemical and pyrolytic products, metabolites, and contaminants is essential for reasonable attempts to anticipate adverse effects. Such data should also permit realistic monitoring in the environment and in animals and in man. Illustratively, the pesticide Captan degrades, possibly thiophosgene, within seconds of contact with serum; monitoring Captan in man or animals is thus inappropriate. Again, polychlorophenols, which are major industrial and agricultural chemicals, yield stable and persistent dibenzodioxins when heated. Some dioxins are highly toxic and teratogenic at the ug/kg level; most dioxins are, however, toxicologically uncharacterized (Epstein, 1970b). Nitrilotriacetic acid (NTA) has been proposed as an alternative detergent builder to polyphosphates in an attempt to reduce cultural eutrophication in lakes and rivers; the current annual usage of phosphates in detergents in the United States is approximately 2 billion pounds. Recent objections to this include the likelihood that the use of NTA will not achieve the stated objective of preventing eutrophication, absence of data on intermediate pathways and reaction products of the biodegradation of NTA, chronic toxic effects of NTA in rodents, the poor biodegradability of heavy metal-NTA chelates (Epstein, 1970d, 1970e), and recent preliminary data on the teratogenicity and toxicity of mercury and cadmium--NTA chelates (Chernoff and Courtney, 1970).

Predicitions of safety should be based on systematic toxicology--acute and chronic toxicity per se, carcinogenicity, teratogenicity and mutagenicity--by appropriate routes of administration in two or more species. Additionally, the development of microcosm or model ecological studies is critical for predictions of environmental safety--an approach which has yet been barely explored.

After the criteria of efficacy, identity, and safety have been satisfied, the new chemical agent may be registered for commerce or otherwise introduced into the environment. Still, the possibility of error due to the insensitivity or unsuitability of toxicological and environmental testing must be recognized. Such a contingency can be minimized post hoc by ecological, monitoring, and epidemiological studies. Monitoring of levels of chemicals or chemical or metabolic degradation products in the environment, and in body fluids or tissues, presupposes the existence of data on the relevance of a particular chemical pollutant to a particular adverse biological effect. Epidemiological surveys should relate to populations at high risk, apart from the general population; such occupational data as currently exists on a restricted basis are virtually inaccessible.

3. Need for Annual Review of Registration:

Registrations for synthetic chemicals should be granted on an annual basis, when they should be reviewed in light of all further evidence that might have developed with regard to human and environmental safety. Additionally, such review should critically examine any new evidence on questions relating to efficacy for established and altered patterns of usage and application.

4. Development of National Data Banks on Synthetic Chemicals:

Standards for drugs are maintained in most countries on a national level and by the World Health Organization in the International Pharmacopoeia. Similar national and international specifications and registers would be highly desirable for all other categories of synthetic chemicals. Data on safety should be collated and distributed nationally and then internationally. These data on efficacy, chemical identity, toxicology, monitoring, epidemiology, and environmental effects for all synthetic chemicals should be analyzed and stored in a manner suitable for rapid access. Various registries, such as the Environmental Mutagen Society Information Center (EMIC), currently deal with different but fragmented aspects of these requirements.

5. Needs to Minimize Constraints Between Industry and Regulatory Agencies:

There is a growing consensus of opinion on the need for legislation to ensure impartial and competent testing of all synthetic chemicals for which human exposure is anticipated. The present system of direct, closed-contract negotiations between manufacturing industries and commercial and other testing laboratories is open to abuse, creates obvious mutual constraints, and is thus contrary to consumer, and long-term industrial interests. One possible remedy would be the introduction of a disinterested advisory group or agency to act as an intermediary between manufacturers and commercial and other testing laboratories. Various legal and other safeguards would have to be properly developed to avoid or minimize potential abuses and conflicts of interest in the operation of this intermediary group. Manufacturers would notify the advisory group or agency when safety evaluation was required for a particular chemical. The advisory group would then solicity contract bids on the open market. Bids would be awarded on the basis of economics, quality of protocols, and technical competence. The progress of testing would be monitored by periodic project site visits, as routine with Federal contracts. At the conclusion of the studies, the advisory group would comment on the quality of the data, make appropriate recommendations, and forward these to the regulatory agency concerned for appropriate action. This approach is certainly more consistent with general industrial practice than is the award of non-bidded or unpublicized contracts. Additionally, quality checks during testing would ensure the high quality and reliability of data, and minimize the need to repeat studies, and thus also reduce pressure on involved Federal agencies to accept unsatisfactory data and post hoc situations. This approach would not only minimize constraints due to special client interests, but would also serve to upgrade the quality of testing in commercial and other testing laboratories.

Additionally, the development of independent non-profit research groups and centers concerned with problems of consumer, occupational, and environmental safety should be encouraged in an effort to develop constraint-free research, consultative and training centers. Universities represent an ideal source of talents in the wide range of relevant disciplines; however, the requisite concept of interdisciplinary programs is still relatively novel to most universities, which are structured on classical departmental lines. The National laboratories should also represent a source of research potential, but under their existing charter they cannot be directly responsive to industrial needs. Further consideration should be directed to the possible need for an independent consumer regulatory or protection agency, and to the development of stronger scientific and legal representation of consumer, occupational, and environmental public interest groups in all agencies concerned directly and indirectly in these areas.

6. Need for Promulgation of Protocols in the Federal Register:

It is critical that Industry, commercial testing and other laboratories be provided with unambiguous guidelines as to exactly what tests are required and as to the necessary protocols for such tests. These protocols should relate to tests for both human and environmental safety, and also delineate principles for interpretation. Concerned parties should be given ample opportunity to challenge or otherwise comment on such protocols before their promulgation is formally ratified. Such protocols should be subject to mandatory annual review.

These procedures will provide a clearer definition as to the precise relative responsibilities of Industry and regulatory agencies in safety evaluation, and thus minimize existing mutual constraints in these areas. Industry will thus know what tests are required, and hence be able to predetermine the approximate costs of such tests, before deciding whether or not to proceed with further product testing and development.

7. Public Access to Data:

Further legislation concerning public access to data is critically needed. All formal discussions between agencies, industry, and expert governmental and non-governmental committees on all issues relating to human safety and environmental quality, and all data relevant to such discussions properly belong to the public domain and should be a matter of open record. Such records, including clear statements, by all concerned, of possible conflicts of interest, should be immediately available to the scientific community, scientific and legal representatives of consumer, occupational, and environmental groups, and to other interested parties. Appropriate legal safeguards for the protection of patent rights should be developed.

In addition to open access of data on all issues of public health and welfare, and environmental safety, it is essential that the interests of consumer, occupational, and environmental groups be adequately represented, legally and scientifically, at the earliest formal stages of such discussions. Decisions by agencies on technological innovations or on new synthetic chemicals after closed discussions on data which have been treated confidentially are unacceptable. Consumer, occupational, and environmental safety apart, such decisions are contrary to the long-term interests of industry, which should be protected from perforce belated objections.

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DETERMINING MAN'S EXPOSURE TO PESTICIDES

Anne R. Yobs, M.D.

Pesticide chemicals are ubiquitous. They have been reported in every part of the natural environment--air, water, soil, crops, food, feeds, and many species of wildlife--and in some occupational settings. The exact pesticide and its concentration in the several parts of the environment varies with time and geographic location as well as with the sampling and analytical techniques used by the investigator. In today's cosmopolitan culture, certain of these chemicals are used to prevent insect damage to clothing and such household items as carpeting and rugs, to control fleas and other insects on pets, to prevent disease spread through control of insect vectors both over land and in airplanes and to control insects as well as rodent damage in the home. Pesticides may even occur in cosmetics which contain oils of animal origin, specifically lanolin.[1]

Pesticides, like many other materials, are subject to being transported great distances once they have entered the air (and atmosphere) or water. Therefore, it can no longer be assumed that exposure will be limited to those chemicals which are being used locally at the time. Exposure to pesticide chemicals can and does occur in the urban situation as well as on the farm, although concentration may be lower in the city.

In order for a material to affect a living organism, it must actually enter the body and be absorbed into it. Pesticides may be absorbed into the human body through the gastrointestinal tract; that is, ingestion; through the pulmonary tract; that is, respiration; and across or through the intact skin; that is, percutaneous. For most of these chemicals, absorption is most efficient following ingestion. For others, however, absorption is just as efficient--and for some even more efficient--when exposure involves the respiratory tree or the skin.

Many approaches have been used in the past in attempts to determine man's exposure to one or more pesticides. These have included the collection and analysis of actual sample meals or meals for a day as was done by Durham and coworkers in 1965.[2] In this study, arrangements were made with participants for two plates to be served at the same time; the contents of one were used for analysis while contents of the other were the participant's meal. The Food and Drug Administration's Market Basket Survey takes a somewhat similar approach to a hypothetical individual.[3] Here the diet of a hypothetical 18-year-old boy is prepared for the table, then analyzed.

There have been attempts to document respiratory exposure by analyzing filter pads from respirators worn during occupational exposure or by measuring the pesticides in the air in the region of the worker's nose and mouth during occupational exposure using a portable micro-impinger or other device and subsequent chemical analysis of the collecting media or solvent.[4] Definition of percutaneous exposure has been attempted through analysis of cloth patches attached to clothing during exposure and extrapolation of this information to determine what total surface exposure would have been under these circumstances.

All of these are so-called direct approaches in that direct measurement of the pollutant itself is attempted in the exposure producing environmental media and under actual exposure conditions. Obviously no one of these approaches measures man's total exposure to pesticides from all routes of exposure, nor are these approaches applicable to a number of individuals in a practical situation. Each, however, is a valuable research tool.

Another approach is the indirect one whereby exposure is estimated by quantitating known effects such as modification of enzyme activity. In order to use this approach, quantifiable effects must be a known (proven) result of exposure, preferably to a single pesticide chemical, and ideally these effects should develop in definite increments as the level of exposure increases. Also, it is necessary for the range of activity under normal or unexposed conditions to be known, relatively narrow and fairly standard with little physiologic variation.

Such effects on humans as are known are usually the same for an entire group of pesticides, such as liver microsomal induction with chlorinated hydrocarbon exposure, or permanent acetyl cholinesterase inhibition with organophosphates but temporary reversible inhibition of the same enzyme after carbamate exposure.

Efforts to identify and document other effects are directed toward study of acutely intoxicated or poisoned individuals and the long-term prospective study of occupationally exposed individuals. Both these groups experience pesticide exposure at a level which is many times that of the general population. It is possible that some effects which develop under these circumstances of heavy exposure may also occur at lesser intensity in the general population. The majority of the long-term prospective or epidemiologic studies of the occupationally exposed are performed in the Community Studies projects.[5] These studies are established by contract with State Health Departments and/or local medical schools in areas of high or unique pesticide usage. Each project has its own pesticide residue analytical laboratory and usually its own facilities for biochemical testing. Subjects are drawn as volunteers from local groups which are occupationally exposed to pesticides. These may be manufacturers, formulators, professional applicators or farmers; a control group of the general population is also followed by each study. Each volunteer, on entering the study, undergoes a complete physical examination including EKG hematology and biochemistry work up as well as appropriate tests for pesticide residue levels--usually in blood--and urinary metabolite excretion; in addition, a complete medical and work-exposure history is taken. These tests and histories are repeated or updated at regular intervals. Data from all projects is then combined for evaluation. From time to time, special efforts are also directed toward study of cellular metaplasia, chromosomal aberration and neurophysiologic changes in these groups. In a nutshell, every effort is made to follow every lead and to develop as many leads as possible. Obviously the study group is primarily, if not entirely, male. Special studies concern other groups - such as neonatal jaundice and maternal-fetal pesticide residue levels. Once again, these techniques are valuable in research but are not suitable for routine use in large groups.

How, then, can one measure or determine the average man's exposure to pesticides in a practical, fairly routine manner that will permit the development of a large mass of valid data over a broad geographic area? The most amenable approach is that in which storage levels of the pesticides and their metabolites are measured or one in which urinary metabolites excretion is measured. Neither of these approaches works for all pesticides nor even for all groups of pesticides.

The chlorinated hydrocarbon pesticides are relatively stable, are lipotropic and tend to be stored in body fat. Therefore, levels in adipose reflect previous exposure to selected ones of the more widely used members of this group - DDT, Dieldrin, the BHC isomers and heptachlor epoxide. From these measurements it is possible indirectly to estimate and compare the previous levels of exposure between groups. Levels in blood are more affected by recent exposures but here the levels are in parts per billion or 10^{-9} grams and consequently fewer pesticides are identifiable.

The presence of DDT in humans was first reported by Lang in 1950[6]. Since that time there have been several reports of studies of pesticide levels in adipose tissue in humans. Usually these have concerned small numbers of individuals in restricted geographic areas[7]. Care must be used in attempting to compare results from one investigator with those of other investigators because of major changes in analytical technology and because of the lack of interlaboratory quality control. At these low levels and with instrumental variation, there is opportunity for rather wide variation of results.

In 1967, a program was initiated to measure chlorinated hydrocarbon levels in human adipose of individuals over the country. This Human Monitoring Survey has functioned with a strong program of interlaboratory quality control and sampling performed according to a statistical design. Therefore, it is possible to compare data with some confidence between years, on a geographic basis, or on age, sex, or racial breakdowns. Eventually, it will also be possible to compare data on the basis of diagnoses, when sufficient numbers of cases have been collected in the various categories and when our data (computer) system is more efficient.

In the occupationally exposed groups it has for some time been possible to measure urinary excretion of DDA, water soluble metabolite of DDT, or PNP (para-nitrophenol) metabolite of parathion. These tests were not applicable to the general population where lower levels of exposure resulted in the excretion of these materials at levels below the sensitivity of the tests, if at all. Recent breakthroughs in analytical methodology development now make it possible to estimate exposure to the organophosphate pesticides as a group by measurement of common metabolites in the urine and to other pesticides such as the carbamates, the phenoxy herbicides, etc. through measurement of the parent compound or phenolic metabolites in the urine. These will be tested in a pilot project to determine their applicability to the general population before launching on a national program.

You may wonder that I have not included measurement of acetyl cholinesterase activity as a monitoring device in humans. The range of normal for this test is quite broad and is subject to considerable individual variation.

The determination of man's exposure to pesticides is important (1) in determining effects of altered pesticide usage patterns, (2) in determining trends and variations, (3) in fully understanding the impact of pesticides on the ecology and (4) in predicting and studying the incidence of health effects of such exposure.

Preliminary evaluation of data from the nationwide survey of chlorinated hydrocarbon levels in humans revealed an unexpected but significant geographic and racial variation in levels of DDT which suggested the existence of another major route of exposure for the general population other than food, most of which in this country is shipped in interstate commerce and so is subject to control of pesticide contamination through a system of legal tolerances. Ambient air was suspected of being this route. There had been little study of pesticide contamination of ambient air. Most work in this field had been problem oriented--that is, study of drift during application or local contamination after application. An energetic program of ambient air sampling at 16 sites over the country has shown considerable geographic and temporal variation of pesticide pollution of air. Such pollution is a potential source of human exposure by respiratory, percutaneous or ingestion and as such would be reflected in the tests which have been discussed.

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PESTICIDE POISONING—A MEDICAL EXAMINER'S VIEW

B.D. Blackbourne

THE COMMUNITY STUDIED

The occupational and community hazards of a potentially lethal agent may be evaluated by studying clinical and fatal cases of poisoning in a community that has been at risk for a period of time. In Dade County, Florida (Metropolitan Miami), a high utilization level of pesticides has existed over many years. Since the origin of the Medical Examiner's Office in 1956, a high percentage of all fatal poisonings have been documented.

In a subtropical area involved to this extent in agriculture, pesticides are very necessary; but, at the same time, potentially dangerous. An estimated 250,000 pounds of organophosphate pesticides are used annually in Dade County.

During the past twelve years, over 100 persons in Dade County have died as the result of pesticide poisoning (Table 1). Over half of these have been suicidal ingestions. Forty-one accidental fatal poisonings have occurred from organophosphate and non-organophosphate pesticides (Table 2). The peak incidence of fatal accidental poisoning occurred in 1963. Through an educational campaign directed toward agricultural users and the community, the number of deaths has decreased in subsequent years (Table 3).

FATAL ORGANOPHOSPHATE POISONINGS

In 1959, the first Dade County death from organophosphate pesticides (parathion) was recognized. In the ensuing ten years, 56 deaths have resulted from these agents. Of these, 28 were accidental poisonings, 26 suicides, and 2 murders.

Eighteen children died from organophosphate poisoning. Each death represented a separate poisoning incident. In several cases, more than one child ingested the poison. But in each case, only one died. Thirteen of the 18 children poisoned were 2 years of age or younger; the youngest was 14 months old; 15 were Negro, 3 were white; 14 were boys, 4 were girls.

Eight of these 18 children found a bag or bottle of concentrated parathion and ate it. Nine other children ingested small amounts of parathion spread about the house, and especially the kitchen, for control of roaches or rodents. One child died of Guthion poisoning.

The disposal of empty metal cans and drums containing any potent pesticides is a very serious problem. Hot water or caustic washing is not sufficient to rid the container of the pesticide. Complete burning of the inner liner and all of the pesticide residue is the only way that these containers may be reused. For routine disposal, cans should be crushed or otherwise damaged (so that they will serve no secondary purpose) and then buried in the ground.

Accidental occupational organophosphate poisoning resulted in three deaths during this study. Two had sprayed with parathion the day prior to becoming ill. The third man had dusted collard greens all day using a rag over his mouth instead of a respirator.

Organophosphate poisoning associated with acute alcoholism resulted in the death of five men. In each case, while highly intoxicated with ethyl alcohol (0.15-, 0.23-, 0.27-, and 0.44- percent ethanol), they picked up a bottle and, expecting that it was more alcohol, drank it.

As with any potent drug or chemical when it becomes available in the community and its lethal poison potential becomes known, those people intent on suicide will use it. Forty-five percent of the organophosphate deaths have been suicidal poisonings.

Two persons with mischief on their minds turned to parathion. One woman put one drop in the beer glass of a loan shark who was extracting $20 a week from her as interest on a $100 loan. When he rapidly died, she pleaded that she had not intended to kill him--only to make him sick. The other case concerned a man who put parathion in his wife's Kool Aid. Admitted to the hospital in such extreme distress that she could not talk, she wrote "poison" and her common-law husband's name on a pad of paper held by a nurse.

NONFATAL ORGANOPHOSPHATE POISONINGS

An estimated 2,000 nonfatal organophosphate poisonings occur yearly in the United States. This figure may be compared with an estimated 200 fatal poisonings. The majority of both fatal and nonfatal organophosphate poisonings occur in Texas and Florida, where large amounts of these materials are used in agriculture. As in all other forms of poisoning, in order to make a correct diagnosis, someone must suspect a toxic agent as the cause. After reviewing the patient's symptoms, the circumstances of his becoming ill, his age and occupation, and available knowledge about the community, the most-likely responsible agents can be selected and laboratory tests performed. Only through rapid and close communication between those having knowledge of the patient and of the circumstances, the physicians treating the patient, and the chemist performing the tests can the correct poison be identified and therapy initiated.

Briefly, the signs and symptoms of organophosphate poisoning are: increased sweating, increased salivation, muscle jerking, constricted pupils, wheezing, severe abdominal cramps, muscle weakness progressing to paralysis, vomiting and diarrhea, cyanosis and convulsions. Of equal importance in suspecting the diagnosis of organophosphate poisoning is the rapid onset and progression of this unusual symptom complex. If pesticide poisoning is not thought of, the illness may be regarded as a primary lung, brain, or heart disease.

NONFATAL PESTICIDE POISONINGS IN DADE COUNTY, 1964-1968

Ninety-two nonfatal poisonings were documented, 79 of them accidental exposures, 11 attempted suicides, and 2 possible attempted murders. Of the accidental poisonings, 26 resulted from occupational exposure and 41 involved children who had ingested or otherwise had been exposed to the pesticide. Of the 79 accidental poisonings, 40 involved parathion, 12 phosdrin, and 5 diazinon.

FATAL, ACCIDENTAL NONORGANOPHOSPHATE PESTICIDE POISONING

After excluding many suicidal poisonings by nonorganophosphate pesticides, 13 cases of fatal accidental poisoning remain in the Dade County files between 1956 and 1969.

The pesticides involved include: those used in building fumigation (4), arsenic (2), tallium (2), phosphorus (3), and paraquat (1).

The first documented fumigation death occurred in 1957--a 27-year old woman. In January, 1963, a home fumigation using acrylonitrile (34 percent) and carbontetrachloride (66 percent) eventually lead to the death of a 41-year-old woman. In December, 1965, a similar situation resulted in the death of a 22-month-old boy. A fourth death related to tent fumigation. A 57-year-old woman alcoholic recently discharged from jail was advised of the plans to fumigate, and said she would pick up her sweater and leave. When the fumigation was completed the following day and the house inspected, the body of the woman was found in the bathroom. Apparently, she had re-entered the house sometime during the night for the purpose of suicide.

Two accidental arsenic deaths have involved small children. The mother of a two-year-old child mixed up some arsenic and water one evening and absentmindedly left it on the kitchen table. The youngster arose before her mother the next morning and drank the liquid, thinking it was water. She lived 24 hours in the hospital. The other child, 17 months old, apparently found a container of arsenic because white powder was noted on his face when he became dizzy and began to cry. He died 2 hours later.

The two recorded victims of thallium poisoning were 3 and 16 years of age, respectively. Their uncle found a gallon jug of light yellow liquid in a ditch beside the road. Thinking that it was motor oil, he took it home. The father of the two victims tasted it and recognized it as honey. If the container had ever been labelled, the label had come off, for there was no warning on the glass jug of the powerful poison it contained. The 16-year-old died 16 days after ingesting the honey, his 3-year-old sister died 4 weeks after eating the same honey. The other members of the family survived.

The three phosphorus deaths include two children and an intoxicated man, who had all ingested phosphorus. They each died from 3 to 9 hours after ingesting the poison.

The single accidental paraquat poisoning involved an alcoholic woman who, while intoxicated, drank a solution of paraquat thinking it was more liquor. Her husband had brought the paraquat home for use in the yard.

WHAT CAN BE DONE

Action to reduce the fatalities and clinical poisonings from pesticides must involve education of the agricultural handlers of pesticides, and also of the general public.

Safety equipment--including gloves, face masks, and protective clothing--have been prescribed for loaders, spraymen, flagmen, and others. This equipment must, however, be used to be effective.

Pesticide container disposal is a problem. Washing with hot water and soap will not remove all of the pesticide residue; the potential for poisoning remains. Large drums may be commercially reconditioned by burning the inner liner. Smaller containers should be crushed or split with an axe so they will serve no secondary purpose and then buried in the ground.

Pesticides are poisons and must be labelled. If removed from the original labelled container, subsequent containers must indicate by prominent label description the nature of the contents. All labels must be so affixed to the container that they will not be rubbed off or washed off by rain. Potent and highly toxic agricultural pesticides have no place in the home. Under no circumstances should pesticides be placed in food containers. No bait made by placing a pesticide on food is acceptable for home use.

SUMMARY

During a twelve-year period in Dade County, Florida, 41 deaths occurred from accidental pesticide poisoning. Twenty-five children were poisoned. Seven poisonings occurred during commercial use of pesticide and 7 involved persons who drank the pesticide while acutely intoxicated on ethyl alcohol.

Five principles are suggested to reduce fatal and clinical poisoning:

1. Observe precautions prescribed for the safe handling of pesticides in agriculture.
2. Make sure that pesticide containers are safely disposed of.
3. Do not take agricultural pesticide home for storage, or for use against household pests.
4. Do not place pesticides on food as bait or in food containers for storage or transportation.
5. Always label pesticide containers so that the label cannot be washed off or rubbed off.

Table 1. Pesticide Poisonings, Dade County, Florida, 1956-1968

	Organophosphate	Nonorganophosphate	Sub total	Total
ACCIDENTAL	28	13	25	41
Children	18	7	7	
Occupational	3	4	7	
Alcohol	5	2	2	
Miscellaneous	2			
SUICIDE	26	46		72
HOMICIDE	2	2		4
TOTAL	56	61		117

Table 2. Pesticides Causing Accidental Death

Pesticide	Number of deaths
Parathion	26
Guthion	1
V.C. 13	1
Methyl bromide	1
Acrylonitrile	3
Arsenic	2
Thallium	2
Phosphorus	3
Paraquat	1
Real Kill	1
TOTAL	41

Table 3. Accidental Pesticide Poisoning, Yearly Incidence, 1957-1968

Year	Fatal	Nonfatal
1957	1	NA
1958	7	NA
1959	5	NA
1960	2	NA
1961	2	NA
1962	1	NA
1963	9	NA
1964	4	22
1965	3	24
1966	2	11
1967	2	11
1968	3	11
TOTAL	41	79

NA--Information not available

Table 4. Nonfatal Pesticide Poisoning, 1964-1968, Dade County, Florida

Accidental poisoning	79
Children	41
Occupational	26
Miscellaneous	12
Attempted suicide	11
Attempted murder	2
TOTAL	92

Table 5. Nonfatal Accidental Pesticide Poisoning, 1964-1968

	Poisoning				Pesticide							
Year	Children	Occupational	Other	Total Accidental Poisonings	Parathion	Phosdrin	Diazinon	Thallium	Phosphorus	Arsenic	Mercury	Other
1964	13	5	4	22	9	1	4	1	2	1		4
1965	10	12	2	24	14	7						3
1966	5	4	2	11	7	3						1
1967	6	4	1	11	5	1				1	2	2
1968	7	1	3	11	5		1				1	4
TOTAL	41	26	12	79	40	12	5	1	2	2	3	14

Table 6. Fatal Accidental Pesticide Poisoning, 1964-1968

	Poisoning				Pesticide			
Year	Children	Occupational	Other	Total Accidental Poisonings	Parathion	Guthion	Acrylonitrile	Paraquat
1964	3		1	4	3	1		
1965	3			3	2		1	
1966	1		1	2	2			
1967			2	2	2			
1968	1		2	3	2			1
TOTAL	8	0	6	14	11	1	1	1

POISON CONTROL CENTERS AND THEIR FUNCTIONS

Henry L. Verhulst

We are now living in an era in which everyone is greatly concerned with the potential danger to our environment from chemical contaminants or additives with which we have constant contact. Some are introduced as part of our manufacturing processes; others by the consumption of products which make our daily tasks easier and our free time more enjoyable. Since most of these chemicals are present in small quantities, their effects, if any, may occur only after long continuous exposure. Since many elements are involved, it may be difficult to recognize the chemical or group of chemicals responsible for a specific illness. Much research is yet to be done, both by Government and the private sector, to determine the hazards and methods of control.

The pediatrician, however, many years ago became aware of the potential acute toxicity of many of these chemicals. This resulted in the development of the Poison Control Center program which I will discuss.

Following World War II, there was a proliferation of new chemicals and new common household products. The names, characteristics, and toxicity of these new chemicals were unfamiliar to practicing physicians. Even the medicines which were their tools had unknown facets when they were ingested in an acute overdose. Manufacturers who might expound on their drugs' therapeutic effects, or reveal their collection of reported adverse reactions, frequently had few data on acute overdosage. These were new problems to the physicians. However, many of the old problems never had been resolved completely, and if they had, this information had not received wide circulation. Among the latter were such questions as, were matches really poisonous, and did shoe dyes actually contain aniline, and if so, which ones; and why tobacco with its high nicotine content was not causing fatalities among children who were ingesting it.

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According to a 1950 survey, over 50 percent of children's accidents reported to pediatricians were due to potential poison ingestions. At the same time, the pediatrician was understandably unfamiliar with such chemicals as sodium tripolyphosphate, ammonium thioglycollate, dimethyldistearyl ammonium chloride, and many other chemical ingredients found in household products. However, knowledge of these chemicals was necessary for the proper treatment of an ingestion.

Because of this knowledge gap and because there were hundreds of thousands of such ingestions annually, the Illinois Chapter of the American Academy of Pediatrics initiated a pilot project in Chicago known as the "Poison Control Center." From its inception the project received the cooperation of the pediatric services in the local major hospitals, the State Health Department, and the State Toxicological Laboratory. With these organizations serving as a catalyst, a working unit was formed representing the local medical society, some 20 hospitals, four full-time health departments, five medical colleges, the Illinois Chapter of the Academy of Pediatrics, and the American Public Health Association.

The Chicago Poison Control Center opened in November 1953. It provided information on and treatment for poisonings, and had the further objective of establishing a program of prevention. The number of other poison control groups which subsequently were organized with the same goals as those of the Chicago Center can be considered a tribute to the latter's success. The new centers soon found, however, that they were duplicating one another's work in compiling information and that some information gathered by one center was not always being distributed to the others. Moreover, clinical and epidemiological information about poisoning experiences were not being collected. It became apparent that some coordination of poison control center activities was necessary.

By 1956, sixteen (16) centers had been established in major metropolitan areas. Most were established by the pediatric service of the childrens' centers in the area. New York City's, the only exception, was placed in the Health Department. The operation of all the centers was fairly uniform. The chief of the pediatric service served as the director. Residents staffed the program and answered requests for information. The hospital assisted in purchasing necessary texts, journals, and special reference material. Descriptions of the first centers made it clear that the program was utilized mainly by physicians treating emergency ingestions.

The poison control movement gained much publicity and resultant popularity throughout the nation. Because of this, many civic organizations as well as medical and paramedical organizations encouraged establishment of poison control centers in local hospitals. Unfortunately, in some instances, the local hospital had insufficient personnel to perform the functions. The community might have had better service had they concentrated on improving the emergency treatment facilities and utilized a center in one of the larger medical centers for informational services.

The designation of poison control centers is made by State Health Departments since medical practice is licensed by the State. However, the individual States have interpreted the guidelines for centers differently. Thus, we have one center in Oregon located at the medical school compared to approximately 100 in the State of Illinois, but, most States have less than twenty (20) centers. The expertise of the staffs of the poison control centers appears to us, and other knowledgeable observers, to increase with the number of calls received. It seems, therefore, that the limited number of centers, designated by most states, would have advantages. We now have a total of 583 designated centers.

The impact of the program to a hospital serving as a center is illustrated by an article on the Boston Center. 1/ It states the number of calls increased from an average of 20 per month in 1954 to nearly 500 per month in 1960. Seventy (70) percent of the calls were from the public. The report also gives information on seriousness of ingestion of 800 cases. Thirty-six (36) percent required no treatment, twenty-nine (29) percent received home treatment, thirty-one (31) percent were treated at the hospital and four (4) percent did not give the information.

The function of the poison control center, then, is to have available information on the formulation of household products or chemicals so information on the toxicity, symptomatology and treatment may be furnished when an emergency occurs. This is not nearly as simple as it might sound. With the exception of medications and a few chemicals which have been ingested frequently, there are limited data except those obtained from animal studies. In many cases, no animal data are available on combinations of chemicals, but only on the individual components. In such cases, only individual data can be given and it is necessary that the physician, or the center, determine the possible extent of the danger. There are some who believe such estimations are subject to many errors. This may be true, but, some action must be taken. Here, the busy center has the advantage since the chance of a previous experience is greater and it can call on past knowledge.

Some of you who have utilized a center are probably concerned by the general nature of the treatment given. There is a mistaken impression that a specific antidote exists for every poisoning. This is not true. In reality, only six or seven specific antidotes are available. Several of these are effective for more than one chemical; still, the number of substances so treated is small. The rest of the information involves symptomatic treatment and contraindications which may be life saving.

I believe it is necessary that we discuss several areas in which poison control centers are of very limited value. First, they are not laboratories to perform chemical analyses on unknown products or gastric contents. The public has an impression that modern science has progressed to a point that the identification of an unknown substance is but a few minutes work. Most of you know this is not correct. It can require many hours or days of experts' time with the most expensive equipment to identify some unknowns. Second, center personnel cannot make a diagnosis that a patient's clinical condition is necessarily associated to a chemical exposure. They can only give the signs and symptoms of a chemical intoxication. The treating physician must decide if the illness is related to the exposure.

Now I should like to discuss the historical evolution of the National Clearinghouse. --

On November 12, 1956, at a meeting of The American Public Health Association, a recommendation was made that a National Clearinghouse for Poison Control Centers be set up by the U. S. Department of Health, Education, and Welfare. This meeting was attended by representatives from poison control centers and from such national organizations and government agencies as the American Academy of Pediatrics, The American Pharmaceutical Association, the Food and Drug Administration, the National Research Council, the Children's Bureau and the Public Health Service. In compliance with the recommendation, the National Clearinghouse for Poison Control Centers was designated as an activity of the Public Health Service in the Accident Prevention Program. It is now located in the Food and Drug Administration, Bureau of Product Safety.

The National Clearinghouse contacts industry for the information that manufacturers and distributors can contribute on their own products. In this way, it is possible to keep track of new products which may be poisonous and of changes in the composition of existing products.

There is increasing willingness by industry to supply information about their products, although the material submitted varies greatly. In some cases we are supplied only formulations. Some furnish expected symptoms and/or treatment recommendations. Fewer supply information on toxicity. However, there has been a noticeable increase in information supplied since the passage of the Federal Hazardous Substances Labeling Act in 1960. Most manufacturers now determine if the LD50 is less or greater than 5 gm/kg., which is the limit set by that Act. Once information on the formulation is obtained, a statement of toxicity and treatment is developed by the Clearinghouse, if one is not included by the Company.

An indexed card file for use of all poison control centers has been distributed. The cards in this file are indexed by trade name and contain such information as composition, concentration, and lethal dose of each specific agent; plus symptoms and treatment of poisoning by the agent. Supplements are sent to the centers as new products come on the market, and as existing products come to the attention of the Clearinghouse. A more extensive card file system is kept at the National Clearinghouse.

A bulletin is published periodically containing trends and statistics obtained from the poison report form analysis. New work done on poisonous or potentially poisonous materials, reports of new treatments for poisonings found in the literature or used by individual poison control centers, interesting cases of poisoning and abstracts from the literature on poisoning are contained in the periodic bulletins.

The Division of Poison Control has developed a reporting system through poison control centers to maintain surveillance of products being ingested, inhaled or absorbed to determine any hazards produced, extent of damage and treatment rendered. The system could better be called a monitoring program since we receive reports only when information is sought from a center by a parent or physician following an exposure. Many cases are treated by hospitals and physicians who already have sufficient toxicity information. Also, we get only limited fatality reports since death may occur days after the ingestion and a follow-up report is not always made. Nevertheless, with 115,000 reports received in 1969 we believe we have a representative cross section of products which are taken by children and those which are causing injury. Semi-annual tabulations are run for internal use by the Food and Drug Administration. Copies are made available to the Department of Agriculture. Individual experience with products is supplied to the manufacturer of a product on request. This system does not provide data about environmental contamination or the possible long term hazard of a chemical. Within the last three or four years there has been, however, a great increase in reports of intentional ingestions. The number of calls requesting treatment information for intentional ingestions has risen steadily to a point where one center reported 50 percent involvement.

Results:

The program has given us information on some real problem areas and removed pressure on others. With a few exceptions, cosmetics have not created a problem. Caustics are still a threat to the health of any child obtaining them, as are some products containing petroleum distillates, particularly mineral seal oil.

Tabulations of reports received in 1969 are shown in Attachment A. These tabulated data have been incorporated onto an automated information retrieval system as the poison control center will receive the results of other cases involving ingestions. This will assist the staff in evaluating literature data and enable poison control center personnel to better evaluate the case before them. This program is now in its pilot stage.

Conclusion:

The present poison control system is designed to supply the treating physician with information necessary to manage the patient who has had an acute ingestion. Although a large percentage of the requests for information still involve the ingestion by children of products, the centers are receiving an increased number of calls for information on intentional poisoning, as we have noted earlier. The majority of the latter appear to be among teenagers. The wide variety of chemicals involved and the dosage range have placed an added burden on the poison control center. The center is unlikely to have case reports of illness caused by long exposure to a chemical since identification of the offending agent is extremely difficult and is likely to be established only if extensive laboratory analytical work is completed. Much work must be done before such data is received routinely.

Reference

1. Robb, Elwood and Haggerty, Evaluation of a Poison Control Center - American Journal of Public Health 53:1751 (November 1963)

ATTACHMENT A

TABLE 1C -

INGESTION REPORTS

PRODUCT	UNDER 5 YRS	5 AND OVER	UNKNOWN AGES	SYMPTOMS UNDER 5
V2 Paint	916	116	108	41
V3 Turpentine	691	78	44	102
V4 Solvents and Thinners	952	214	181	145
V5 Oil paints, stains & preservatives	251	43	35	10
V6 Glues & Adhesives	1,280	170	118	97
XX Unknown	481	875	96	52
X1 Veterinary products	445	37	44	20
X4 Pesticide combinations	16	20	9	3
X5 Household product combinations	167	100	54	19
X6 Medicine combinations	1,220	4,517	319	177
X9 Miscellaneous products	1,022	276	214	67
02 Tobacco	229	6	13	12
03 Alcoholic beverages	58	105	8	27
04 Children's Paint, Crayons, Modeling Clay	431	38	43	3
05 Venom - Snake or Spider	226	727	454	93
06 Ink	344	124	52	17
07 Matches	374	13	28	5
08 Fertilizers, Plant foods	392	86	53	19
09 Chemicals	672	496	304	63
10 Antiseptic medication	973	285	122	53
11 Liniments	1,171	269	110	109
12 Eye, Ear & Nose preparations	388	18	31	23
13 Ointments	481	22	36	6
14 Dental Preparations	253	51	35	13
15 Camphor products	239	71	33	40
16 Medicated lotion & creams	161	27	24	5
17 Topical baby preparations	508	6	42	18
19 Miscellaneous external medicines	916	172	106	75
2X Antihistamines & cold medications	2,118	459	104	200
20 Baby aspirin	10,690	504	146	358
21 Adult aspirin	1,115	842	78	40
22 Aspirin, unspecified type	2,689	1,501	93	102
23 Miscellaneous analgesics	1,511	2,260	230	105
24 Laxatives	859	103	34	61
25 Barbiturate sedatives	431	2,152	143	109
26 Non-barbiturate sedatives	238	2,526	263	48
27 Cough medicines	1,058	134	50	167
28 Internal antibiotics	701	178	57	28
29 Psychopharmacologic agents	1,915	4,062	406	420
30 Anticholinergics, antacids	542	136	38	56

-1969

- BY CATEGORY

SYMPTOMS 5 & OVER	SYMPTOMS AGE UNK	HOSPITAL UNDER 5	HOSPITAL 5 & OVER	HOSPITAL AGE UNK	FATAL ALL AGES
28	28	10	5	2	-
13	4	81	9	1	-
66	41	81	32	3	6
15	4	4	2	1	1
48	11	13	9	-	-
388	25	33	413	15	13
6	1	8	2	-	-
9	4	4	3	-	-
54	14	7	27	-	3
2,613	138	143	2,203	45	27
57	21	17	9	-	1
2	-	2	-	1	-
66	3	11	32	1	-
1	2	2	-	-	-
322	178	3	19	-	1
11	-	1	1	-	-
1	1	-	-	-	-
9	5	6	-	-	1
107	48	29	36	4	6
45	9	23	20	2	1
94	11	49	71	4	4
1	2	6	1	-	-
1	1	2	-	-	-
10	4	3	1	1	2
18	7	48	12	2	-
5	1	3	-	-	-
-	2	3	-	-	-
43	5	24	17	1	1
161	15	78	80	2	-
25	8	471	20	5	5
206	19	56	179	3	5
367	11	169	421	9	5
857	67	69	628	15	8
10	3	18	5	-	-
1,513	76	84	1,321	38	26
1,528	94	25	1,201	28	17
53	9	50	12	2	-
50	9	11	34	4	-
2,128	119	275	1,743	55	16
59	5	30	37	2	-

TABLE 10 -

ATTACHMENT A (Continued)

INGESTION REPORTS -

PRODUCT	UNDER 5 YRS	5 AND OVER	UNKNOWN AGES	SYMPTOMS UNDER 5
31 Diuretics	331	[illegible]6	17	20
32 Iron preparations	403	51	24	48
33 Vitamins, minerals	3,850	551	186	114
34 Hormones	1,566	212	95	37
35 Cardiovascular medications	480	120	30	53
36 Amphetamine type preparations	915	393	92	196
37 Antidiarrheal agents	375	30	20	60
38 Vernifuges	151	37	22	9
39 Miscellaneous internal medicine	2,403	1,762	293	231
40 Household bleach	1,828	318	185	149
41 Household disinfectants & deodor.	2,397	177	264	135
42 Corrosive acids & alkalies	1,332	343	245	513
43 Solid polish or wax	75	6	11	5
44 Dry cleaning fluids, spot removers	147	69	47	23
45 Soaps, detergents, cleaners	3,199	334	414	265
46 Shoe preparations	254	24	29	15
48 Liquid polish or wax	1,084	68	102	113
49 Miscellaneous household products	495	75	82	17
50 Kerosene	542	47	32	185
53 Lighter fluids	1,039	72	80	175
57 Gasoline	744	384	120	165
58 Petroleum solvents & cleaners	253	30	34	40
59 Miscellaneous petroleum products	744	79	86	73
60 Fingernail preparations	721	33	45	41
61 Perfume, cologne, toilet water	1,975	50	104	86
62 Personal deodorants	191	27	21	13
63 Hair preparations, except shampoo	553	64	65	32
64 Cosmetic lotions and creams	970	55	97	51
65 Hair shampoo	208	16	14	11
69 Miscellaneous cosmetics	491	16	38	29
70 Insecticides	1,855	549	525	142
71 Rodenticides	960	136	96	23
72 Fungicides	52	20	18	2
73 Herbicides	121	75	85	16
74 Moth balls	700	43	70	19
75 Animal repellents	76	43	42	23
76 Insect Repellents	172	39	25	23
80 Carbon monoxide	30	153	41	15
81 Gases, Vapors, Fumes	31	213	177	13
90 Mushrooms, toadstools	499	65	56	10
91 Plants	2,819	630	485	124
Total all cases reported	76,155	31,274	8,872	6,322

Source: Individual poison reports (phone inquiries and treated cases) submitted to by 439 centers in 46 states.

1969

- BY CATEGORY

SYMPTOMS 5 & OVER	SYMPTOMS AGE UNK	HOSPITAL UNDER 5	HOSPITAL 5 & OVER	HOSPITAL AGE UNK	FATAL ALL AGES
10	-	19	6	-	-
4	2	112	6	3	2
26	9	58	5	-	-
24	8	25	15	-	-
29	6	49	38	3	3
180	33	97	89	6	3
9	4	49	2	1	3
3	-	3	1	-	-
819	77	137	541	23	8
62	21	43	32	2	-
26	17	37	14	3	-
173	73	273	71	6	4
-	-	3	1	-	-
31	7	9	19	-	1
48	41	58	24	6	-
2	3	6	1	-	-
10	7	119	7	1	2
11	5	7	-	-	-
13	5	185	11	2	2
12	15	110	5	2	2
97	24	119	27	1	-
10	7	26	6	1	-
12	7	57	4	-	1
1	1	3	3	-	-
4	4	16	-	-	-
8	1	1	-	-	1
10	8	7	3	-	1
3	4	5	3	-	-
1	1	2	1	-	-
8	1	4	2	-	-
186	119	107	100	13	14
29	8	76	28	2	6
3	3	3	-	-	-
23	30	6	10	-	6
3	5	18	2	-	-
26	12	1	-	-	-
8	6	4	1	-	-
103	19	2	52	1	4
140	70	7	32	3	3
7	7	8	10	1	-
114	42	21	31	1	1
13,278	1,717	3,844	9,808	327	216

the National Clearinghouse for Poison Control Centers

United States Department of Health, Education, and Welfare
Public Health Service, Food and Drug Administration

THE INVESTIGATION OF A FIELD PROBLEM OF AN UNKNOWN ETIOLOGY

EARL EDSEL MOORE

This paper will be primarily directed to pesticide-environmental incidents and situations but occasional reference will be made to pesticide human exposure considerations.

The safe and proper use of pesticides is of major interest to everyone and especially to those State and Federal Agencies with pesticide regulatory responsibilities.

These agencies must deal with a multitude of situations that may involve contaminated foods, goods, environmental or other detrimental conditions; it is therefore imperative that swift and proper action be implemented to adequately safeguard public health and for the preservation of a quality environment.

The proper documentation of pesticide accidents and incidental contamination as a result of faulty or indiscriminate use can serve as a useful basis for developing preventive measures in pesticide use considerations. The facts uncovered by a thorough investigation of a pesticide oriented problem can be translated into vigorous educational programs.

Numerous incidents occur yearly in which a pesticide is implicated or suspect. These may be accidental human exposures occasionally resulting in death, crop damage, fish and wildlife kills, a contaminated water supply, a contaminated livestock feed, and many other related incidents.

It should be clearly understood there is no magic formula in conducting field investigations that would apply to all circumstances as there are too many variables and possibilities. For instance the investigation of a pesticide human exposure would necessitate a different approach than perhaps an environmental occurrence. However, there are certain basic principals than can be observed and applied when a pesticide is implicated or suspect.

The principals of basic epidemiology that are appropos in the investigation of any disease or trauma effecting a certain locale and population are also acceptable and appropriate for pesticide incidents.

A thorough epidemiological investigation should determine the who and what was involved. The who (host) may be man, animal, wildlife, water supply, crop, etc., and the responsible agent (what ? Pesticide), and the environmental situation which may have contributed to the occurrence of the incident, (such as a misuse, improper protective clothing, run-off in a water supply, spray drift, etc.).

Proper evaluation of the information gathered in an investigation can serve as an instrumental tool in developing programs to abate reoccurrences.

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These have been employed very effectively for decades by public health agencies in the control of communicable diseases, food borne outbreaks, epidemics, chronic disease and others.

It is most essential to understand that all pesticides are toxic chemicals and by necessity are poisonous in order to kill pests. They are capable of producing illness of varying degrees and even death to man, animals, and wildlife when indiscriminately used. The extent and severity of morbidity or mortality will depend on numerous factors including the toxicity of the pesticide, route of exposure (oral, dermal, respiratory), the susceptibility or sensitivity of the person (s), animal (s), or wildlife involved and others. Individual reactions will also vary depending on environmental factors such as temperature, humidity, and diet, and intrinsic factors such as age, race, sex, physiological activity, subclinical pathology, fatigue, etc. In simple terms this implies all living creatures possess a different sensitivity level as to the degree of exposure that produces or constitutes illness or death.

In retrospect to these variables, trends are somewhat apparent in most poisoning or environmental investigations. The time interval between exposure and the onset of symptoms (referred to as the incubation period) is generally short. Naturally such is much more pronounced where humans and animals are involved, (by the same token 2, 4-D drifting on a tobacco or tomato field would produce adverse effects rapidly.

The manifestation of most acute exposures to humans will produce symptoms within a few minutes (there are, of course, exceptions, for instance Paraquat, a defoliant herbicide has an incubation period of 7 to 21 days). As expected a concentrated solution will produce clinical symptoms more rapid than a diluted one, and an oral exposure will generally produce earlier signs than a dermal exposure.

An investigation of a human poisoning and particularly occurrences involving foods and environmental contamination may necessitate the cooperation of several people and/or agencies Most important is the cooperation and suppprt of a competent Toxicology Laboratory (Pesticide residue detection). Most investigations especially those of an environmentally oriented nature, will require the collection of samples for analysis, and without adequate sampling of specimens, and a reliable analysis, very little may be accomplished.

Considerations in Conducting Pesticide Field Investigations.

Perhaps one of the most important points to emphasize is the investigation should be inaugerated as soon as the incident is reported for several reasons:

1. This practice may enhance an opportunity to witness the actual condition (s) or situation. For instance, spray drift from an airplane may have caused crop damage and of less significance than reported. There may be other extenuating circumstances to the problem.

2. Presents a better opportunity of learning all the details encompassing the incident. Memories are often short and important points may be overlooked, should sufficient time elapse.

3. In the event the incident warrants the collection of environmental sample (s), it is likely the sample (s) will be of more value than if a significant amount of time has elapsed. The situation may be subject to change, depending on the environmental conditions (naturally there will be instances when the investigator has no control of this because of delayed reporting). For example - a report is received that an airplane had sprayed chemicals near a farm pond. No fish died, yet [illegible] could not drink the water. Three weeks elapsed before the incident was reported. It may be impossible to establish a hazardous condition ever existed.

4. The investigation should be detailed and thorough especially those involving environmental situations. There may be subsequent legal action and the investigator may be subpoenaed to testify in court and the report of the investigation (or portions) may be introduced as admissible evidence.

5. When determined applicable, camera snap shots, preferably color slides (Polaroid may be suitable in certain situations) are an excellent illustration of property damage, and actual conditions at the time of the investigation.

6. The investigator should always be prepared to collect samples for analysis if applicable. It may be feasible to determine the necessity at the time of reporting and the tools and type of containers required for collection. This would depend largely on the nature of the incident. Samples should never be accepted from an unauthorized person or agency. (Such would not be acceptable should legal proceedings subsequently develop). The laboratory should be alerted that samples may be collected for analysis in order to acquire the results as soon as possible.

The investigator may find it desirable to attempt to determine the agent (Pesticide) involved or suspected at the time of reporting. This would present an opportunity to become familiar with the classification and toxicity and other characteristics of the chemical such as persistence which may be of value in conducting the investigation. For example, a farm owner reports an Aerial Applicator sprayed mosquitoes with Malathion near his farm pond and two weeks later the fish suddenly die. The investigator then should consider and look for other causative agents because Malathion has a low order of toxicity and is nonpersistent.

What then is the type of information to be documented, and what should the investigator look for, questions to ask and data to record? This is somewhat dependent on the nature and severity of the incident. It is likely environmental incidents will require a more comprehensive investigation and consequently the discussion is directed accordingly. Reports should be written promptly, and the investigation and occurrences should be listed in sequence. The development of a form or format in collecting the information would be helpful. This is not construed to be a complete listing nor necessarily in order of priority.

1. Record the date of occurrences of the incident, the exact time it is reported and by whom, their phone number and address. Request specific directions to the scene to prevent any delay.

2. Contact the local health agency or other State or Federal Agencies that may also have some responsibility to the problem (transportation spillage accidents, fish kills, contaminated food moving in interstate commerce, etc.). In certain instances when a causative agent is suspected and represents a detrimental effect, the investigator should be prepared to advise a quarantine (pending on investigations and a laboratory analysis of samples) provided the person reporting the incident has the authority to invoke such action to abate further contamination or hazardous conditions.

3. After arriving at the scene should more than one individual be acquainted or have knowledge of the incident, interviewing all connected persons should enhance a better representation of what developed and transpired. Secure names, addresses, and phone numbers, as it may be necessary to reestablish contact at a later date to clarify a point.

4. Describe the nature of the problem and record the environmental situation (s) encompassing the incident. (If applicable).

5. Attempt to determine the source of contamination and the causative agent (s) as soon as possible. This may be very important in preventing further possible detrimental effects. Appropriate specimen collection apparatus should have been brought along.

6. For on-the-farm problems (such as livestock kill, crop damage, or contaminated feed stuffs) record the pesticides or toxic agents that have been used recently and last date of application, rate and method application. It may also require securing similar information from a neighbor (s).

7. The evaluation of habits of pesticide usage, storage, (where and how) and disposal of empty containers may be of value in determining the cause of the incident and possibly where the fault lies.

8. In instances when a pesticide is suspect or implicated record name of pesticide, formulation, active ingredients, manufacturer, size of container, amount used. A copy of the label of the actual container may be helpful. Secure a copy of invoices, bill of lading, or any other document which may be associated with or conceivably have bearing on the incident.

9. List species of animal (s),wildlife, crop (s), or portion (s) of the environment affected. Record the visible effects as they exist and are observed.

10. Record route of exposure to animals or wildlife (dermal, oral, respiratory) and directly or indirectly such as an application or consumption of contaminated goods.

11. Record time lapse between exposure and onset of symptoms, hours, days, etc., and the duration of exposure provided this can be validly established.

12. In instances involving animals and wildlife, record the number affected, number expired, and number recovered.

13. Treatment (if any, what and by whom).

14. Upon conclusion of the investigation, should the investigator consider it necessary and has the authority, quarantine action should be inaugerated to prevent any further detrimental effects to public health or the environment (if not previously accomplished).

There will be other details dependent on the occurrence as there are a multitude of variables and each occurrence in all probability will be somewhat different, nor will particular situations require collection of all of the suggested data. It should be emphasized that often the investigator fails to document sufficient detailed information when conducting the initial investigation, usually necessitating a return visit. Since conditions are subject to change, it is imperative to conduct a thorough investigation on the initial visit.

The proper sampling of specimens for pesticide analysis is extremely important. For without a representative sample (s) collected in the proper amount, in the prescribed manner, and the appropriate container, it will be of little value. The source of the problem may not be determined. In fact the success of the investigation may impinge on the samples collected. Only brief reference will be made to specimen collection as "Sampling Procedures" are scheduled for discussion later in the course.

1. All specimens should be placed in chemically clean containers provided by the testing laboratory. (Never put specimens for pesticide analysis in plastic containers). If applicable use chemically clean tools (scoop, bucket, cup, etc.) in collecting the specimen (s).

2. The sample should be representative of the contaminated media.

3. All samples should be properly identified.

4. Provide the laboratory analyst with a brief resume of the incident and if possible a clue to the pesticide (s) to analyze for. Remember the analyst does not have the benefit of the knowledge of the investigator.

5. Submit the samples as soon as possible after they are collected.

To emphasize the value of gathering detailed information and drafting a comprehensive report, following are reports of two actual investigations illustrating the importance of many of the foregoing referenced points.

These may also serve as an aid in conducting investigations of a similar nature.

ABSTRACT OF A FIELD INVESTIGATION TO LOCATE A CONTAMINATED DAIRY HERD AND ISOLATE SOURCE OF CONTAMINATION

EARL EDSEL MOORE

This is an account of an investigation and subsequent developments of an actual occurrence to locate a dairy farm producing a contaminated milk that was being shipped interstate to the Cincinnati, Ohio Milk Shed in April 1969 and to isolate source of contamination. The names and firms of the involved in this investigation have been excluded.

The investigation reflects a sequence of events by both the Food and Drug Administration and the Kentucky State Department of Health.

On April 2, 1969 the Cincinnati Regional Office of the United State Food and Drug Administration notified the Kentucky State Department of Health that a violative level of Dieldrin had been detected in a sample of large curd creamed cottage cheese manufactured by a local firm. The discovery occurred as a product of the Food and Drug Administrations Established Routine Food Basket Survey and Surveillance Program (compliance of permissable pesticide residues in foods). A Food and Drug Official disclosed the detection occurred on March 16, 1969, and that subsequent investigations revealed the source of contamination was fluid milk originating from a route that involved 12 Central Kentucky Milk Producers. Furthermore, a Food and Drug Administration Inspector had been dispatched to begin sampling individual producers on the route on March 31 to determine the source (s) of contamination.

On April 3rd a State Department of Health Investigator accompanied by the milk hauler, covering the route, began sampling the 12 milk producers on the route in a cooperative effort with the Food and Drug Administration to determine the source (s) of contamination. The samples were submitted to the State Department of Health Pesticide Laboratory for analysis the same day.

While collecting the milk samples from the 12 farms, a detailed inquiry regarding pesticide usage on the farms during the last year indicated there did not appear to be any misuse or faulty storage.

Meanwhile the Food and Drug Administration had advised the Cincinnati Department of Health of the problem. The Kentucky State Department of Health, the Food and Drug Administration, and Cincinnati Officials collaborated and accordingly placed the 12 farms under official quarantine. Preventing further shipment and sale of the milk either interstate (March 31) or intrastate (April 2).

In the late afternoon of April 3rd, Food and Drug Officials notified the State Department of Health that samples collected by their field inspector from the milk producers were free of contamination except one. The sample was from a producer with a 105 cow herd. Feed samples collected on the farm on March 31 by the Food and Drug Administration were void of contamination.

The quarantine on the remaining 11 herds was rescinded on the evening of April 3rd by the State Department of Health.

Due to the high level of Dieldrin in the milk of the affected farm, the investigator revisited the farm on April 4th to sample all feeds in inventory, water, and forage to which the milking herd had been exposed to determine the source of contamination. The samples were submitted to the State Health Department Pesticide Laboratory the same day. During the revisit the proprietor of the farm reinterated that neither Dieldrin or Aldrin (metabolized to Dieldrin by the human and animal body) had been used on the farm, and that pesticide application was accomplished by a custom applicator on crop land far removed from areas in which the producing animals had access.

Furthermore, the investigator was advised that the farm had purchased 35 head of dairy cattle and most had been incorporated into the milking herd about February 28.

The milk samples collected on the 3rd by the investigator were reported to be free of contamination except one by the State Health Department Pesticide Laboratory and it contained a comparable level of Dieldrin (as reported by the Food and Drug Administration).

The herds were segregated on April 5 to determine the feasibility of the new herd being the contaminating source. A composite sample from each group revealed the level to be comparable, indicating that either or both a feed stuff or water could be the contributing source.

On April 15 the laboratory reported all feed, water, and forage samples collected on the farm were void of any Aldrin or Dieldrin contamination. Subsequent milk samples from the combined herd on April 10th and 11th revealed the level of Dieldrin to be declining, indicating the animals were not being subsequently exposed. Consequently, it could be concluded that a contaminated feed must have been feed prior to March 31, 1969 (the day the Food and Drug Administration collected samples of farm feeds, etc.).

The milking ration for the dairy herd was prepared on the farm and numerous ingredients were purchased from several sources and rather frequently, in fact, all of the raw ingredients sampled on April 4th had been in inventory for 10 days or less (except a small quantity of ear corn purchased in Indiana). These were transported to the farm in the farm truck.

During a revisitation to the affected farm on April 16, the proprietor of the farm disclosed the source of two of the raw ingredients (bagged soy bean and cotton seed oil meal) was purchased from a local grain firm that retailed and warehoused pesticide products. This was not the case with the other two sources of ingredients. It was suspicioned that possibly as a result of faulty warehousing or handling that raw ingredients purchased from the firm may have been accidentally contaminated. An inspection of the facilities failed to indicate this feasibility.

The visit and inspection, however, proved to be valuable. The manager of the firm disclosed that the affected farm had purchased a quantity of feed oats for incorporation in the milking ration, but from another local grain supplier that was the low bidder. Furthermore, the oats had been purchased prior to the detection of the contaminated milk by the Food and Drug Administration.

A visit with the manager of the local firm, reportedly supplying the oats, verified the purchase but that the firm had acted only as the intermediary in the transaction. Three hundred bushels of oats were purchased on February 28, 1971 from a Louisville Based Grain Elevator, delivered the same day to the affected farm in a truck owned by the local firm. The purchase invoice, however, bore the name of the local firm.

Returning to the farm late the 16th, the proprietor admitted mention of the oats had been overlooked during the initial investigation. The oats had been incorporated into the milking ration beginning about March 3rd and the supply exhausted about March 25th. Furthermore, it was believed none of the oats remained in inventory, however, an inspection revealed there was some eight to ten bushels in the storage bin.

A representative sample from the lot was collected and submitted to the Kentucky State Health Department Laboratory and subsequently reported to contain a violative level of Aldrin. Thus the contaminating source was officially isolated by the Health Department on April 28, requiring some 24 days (April 4 - 28) in the process. Hence, the initial and subsequent investigations were an important basis to determine the actual period of contamination of the herd (March 3rd through March 25th), and the amount of contaminated milk that was marketed. The time period of March 4th (in all probability when the Dieldrin began to appear in the milk) and March 31st when the quarantine became effective. It was calculated some 108,000 pounds of contaminated milk were marketed (27 days, herd average 4,000 a day)

Since the oats contained a violative level of Aldrin, and also subject to Provisions of the Kentucky Food, Drug and Cosmetic Act, further investigation was required.

An investigation of the originating source of the oats, a Louisville Grain Elevator, was begun on April 28. Approximately 10,600 bushels were in inventory and were promptly placed under quarantine. Officials of the firm believed the 300 bushels purchased by the affected farm may have been a part of approximately 30,000 bushels of oats that had been received between February 11, 1969 and April 1, 1969. The oats were procured from a Grain Elevator in Indiana and reportedly came from several growers over a multi-state area prior to and during the time period specified above. Nineteen thousand bushels of the lot had been sold almost exclusively to three poultry farms in North Carolina and Georgia. Other than the oats in question, less than a hundred bushels had been sold locally.

Representative samples from six bins from which oats were stored were collected and submitted to the State Department of Health Pesticide Laboratory for analysis. On May 5th the Pesticide Laboratory reported the oats to be void of contamination. Consequently it was impossible to establish what portion of the 30,000 bushels were contaminated. Because of elapsed time between purchase of the oats by the affected farm and detection as the contaminating source (February 28 through April 28), Food and Drug Administration Officials in North Carolina and Georgia (which had been alerted on April 28) disclosed that interstate investigations did not uncover any contaminated oats. Adulterated foods or feeds moving in interstate commerce are the responsibility of the Food and Drug Administration.

The quarantine on the oats in inventory was rescinded on May 5th by the State Department of Health.

The affected farm was required to destroy the milk produced from the herd covering an 84 day period (March 31 through June 22) or until the level met the zero tolerance established by the Food and Drug Administration. The milk producer experienced a substantial loss during this time period which amounted to approximately $24,000.

Since the State Health Department investigation revealed the farmer was not at fault because of faulty use or storage, he was eligible for restitution for a portion of the loss through a Federal Government Disaster Program. Additionally, the Cincinnati Milk Shed absorbed a portion of the loss, however, combined, both were not sufficient to account for the entire loss suffered by the producer.

The producer subsequently instigated legal proceedings against the local grain firm and the Louisville Grain Elevator for restitution for the remainder of the loss of the milk.

Council for the defendants reviewed the dossier of the investigations, laboratory analysis, and all other pertinent information encompassing the incident. The attorney disclosed the evidence would disfavor his clientele in court. Consequently, the deficit, (some $1,650) was remunerated to the milk producer.

AN ABSTRACT OF A FIELD INVESTIGATION TO DETERMINE THE CAUSATION OF MORTALITY IN A BEEF HERD

During the late afternoon of August 19, 1970 the Director of the Kentucky State Department of Agriculture's Diagnostic Laboratory notified the Kentucky State Department of Health that a small Western Kentucky Beef Cattle Producer had mysteriously lost 14 head of breeding stock in less than a 24 hour period. Additionally, the herd veterinarian was unable to establish the cause for the sudden mortality which occurred on August 18th. However, the veterinarian felt a toxic material was involved after performing an autopsy. Furthermore, there was suspicion that a stream running through the farm from which the animals drank was contaminated with a pesticide.

The affected producer disclosed in the investigation instigated on August 20th, that on checking the herd on the morning of August 18, ten animals were found dead in the pasture field, four were very ill, eight others appeared to be slightly ill, and the remainder appeared normal. They were droopy, lethargic, generally weak, ataxia, and had diarrhea. It was reported the other sick sanimals died later on the 18th and had tremors and muscle twitching, in addition to the above symptoms. According to the owner a treatment of atropine sulphate was administered by the herd veterinarian which is the treatment or antidote for poisoning by organo phosphate and carbamate insecticides. However, the ill animals failed to respond, and it was later discovered this was an improper treatment. It could not be determined what effects, if any,this constituted to the other recovering animals.

The owner disclosed that pesticides had not been applied to any fields or forage (the only diet) to which the animals had been exposed. Samples of forage from the pasture field and from the suspect stream were collected for pesticide analysis. Adjoining farm owners, with cattle drinking from the same stream, reported no sick animals or losses.

An inspection of pesticide storage on the affected farm revealed a few pesticides which were occasionally used on field crops, mainly tobacco. A half gallon container of Toxphene was noticed, which no longer is recommended for tobacco. The owner disclosed that the insecticide was purchased on August 15th from a local firm for the purpose of spraying the cattle for fly control, and had used Toxaphene for several years without any ill effects. Less than a quart had been used, and he was sure this was not the causative agent.

The cattle had been congregated on the 17th, however, 12 were not sprayed because of darkness. Ill effects were not noticed until the next day and because of the illness and death in the herd, the owner decided not to spray the remaining cattle.

The owner stated he had followed label directions on the Toxaphene container with the exception of incorporating approximately a half gallon diesel fuel with the spray mixture to enhance the residual period (only water was recommended).

The supposedly diesel fuel had been poured from an unlabeled one-gallon brown-colored glass container. However, an inspection did not reveal that type of odor or exact appearance.

A sample was collected from the Toxaphene container to analyze for possible cross contamination as a result of faulty manufacturing. Samples were also collected of the spray mixture remaining in the spray tank, the one gallon container, and specimens from two organs of one of the expired animals.

The animals were quarantined pending laboratory analysis to determine the causative agent.

On August 27th the Pesticide and Chemistry Laboratories reported the samples of forage and water were void of contamination and the Toxaphene was not cross contaminated. Furthermore, the spray tank sample and especially the gallon glass container (supposedly Diesel Fuel) contained high levels of arsenic. The tissues also contained a lethal level.

It was subsequently established that Sodium Arsenite was the pesticide in the unlabeled glass container.

The spray solution apparently caused skin irritation, consequently, the cattle licked their coats ingesting lethal levels of the arsenic containing compound.

In a later discussion the owner denied purchasing the pesticide, much less storing in an unlabeled container. Furthermore, that he had personally procured the gallon of diesel fuel and put in the unlabeled container and stored in the exact location as the contaminated container. The owner declared since sodium arsenite was found, someone had maliciously switched containers.

The fact remains, had the farm owner strictly adhered to the label directions, the incident would not have occurred. The loss of the cattle was estimated at $4,000, indeed an unfortunate and expensive mistake. Since the incident was a result of misuse the producer was not eligible to receive restitution from any disaster programs.

Since the quarantine of the herd represented a substantial daily loss to the producer a field experiment was proposed by dairy specialist of the Department of Animal Science, University of Kentucky, to the owner to accelerate the removal of the Dieldrin residue from the contaminated dairy herd. This involved the feeding of Phenobarbital and activated carbon to the affected herd.

The treatment process[1] was apparently effective in reducing the Dieldrin level. After one week of treatment, residue had declined about 64% compared with 36% for the control group. At 22 days milk residue in the treated group was about one half that of the control group. The time during which the milk had to be withheld from market was shortened by at least one month for the treated group.

REFERENCE

1. D. G. Braund, B. E. Langlois, D. J. Conner, and E. E. Moore, 1971 Feeding Phenobarbital and Activated Carbon to Accelerate Dieldrin Residue Removal in a Contaminated Dairy Herd. Journal of Dairy Science, volume 54, No. 3, Pages 435-438.

INTRODUCTION TO CHEMICAL ANALYSIS FOR PESTICIDES

L. A. Richardson

An introduction to pesticide residue analysis can be divided into three major categories: essential background information, preparation for analysis, and the actual analysis.

In the first category, one finds classifications systems, chemistry of the compounds, sources of contamination, and incidence and contamination levels. Both the use and chemical classifications are valuable to the analyst in making the initial decision as to the type of possible exposure. Whether the sample was exposed to insecticides, herbicides, or fungicides, or all of these, will assist in formulating the analytical scheme and the methodology required for analysis. A knowledge of the chemical classification will allow one to further define the potential contaminants and thus serve in the selection of the analytical scheme. Sources of contamination and incidence in the particular media in question also influence this decision. Chemistry of the potentially contaminating compounds is extremely important in that one must decide whether to look for only the parent compound or its metabolites, degradation products, or reaction products. Without a knowledge of the chemistry, this decision cannot be made. The level of contamination expected will influence not only the previously noted decision but the sensitivity requirement of the methodology utilized.

The reasons for doing residue analysis are varied and are important information to the analyst. In any given situation, one must know if the prime interest in in identification or quantitation of parent compounds or both these definitions. Perhaps the identity is already available, thus only quantitation is important. In this case, the level of detection is of interest and the sensitivity of methods are important. In other situations we may be most concerned with measuring degradation, reaction, or metabolism products. Here, we are very much concerned with identification as well as the level of detection. Perhaps we should look at some of the reasons for residue analysis.

For some, it is a matter of protecting the public health. I'm sure that you have been introduced to the toxicity of these materials in large concentration and the potential problems which may arise from even small dosages. Under toxicity, we can speak of two subcategories, the somatic effect, or the effect upon human health and longevity, and the genetic effect, or the potential effect of these materials on reproduction and the characteristics of the resulting offspring. The genetic effect is a more subtle or sinister potential effect of chemical agents in general and in our discussion, pesticides in particular. Many of the agents which we use as pesticides have been shown to accumulate in the fatty tissue of living organisms and to reach relatively high proportions in other tissues. This is an additional point of concern in the more subtle or sinister potential effect of pesticide agents. Consequently, we see that additional information must be gained on each of these pesticides and their metabolites from the standpoint of public health. Very low level quantitation and absolute identification are both essential in this work.

Regulations which have been established for pesticide residues, aimed specifically at the protection of public health, is only possible through residue analysis. Consequently, we must enforce the regulations, and this enforcement must be supported by data obtained in the chemistry laboratory. A fringe benefit of the enforcement of regulations and the investigations of pesticide residue effects consists of information on incidents and concentrations of residues. In essence, we are providing a sort of monitoring even though this may not be the principal reason for the residue analysis.

Residue analysis is also a very large part of pesticide research. The development of efficient pesticides depends heavily upon not only residue methods but upon pesticide methodology development in general. Improved methodology in particular requires a considerable effort on the part of the residue analysis and a tremendous number of analyses. In our work we are making a concerted effort to investigate the effect of pesticides on the human animal. We are concerned about which pesticide agents are present in human tissue and the concentrations of these agents. We are also interested in pesticide metabolism. Some agents metabolize to relatively safe material as is the case of DDE, a nontoxic compound resulting from the metabolic conversion of DDT. On the other hand, heptachlor epoxide results from the metabolic conversion of heptachlor and is just as toxic, if not more so, than the parent compound. Analytical methods themselves are based upon the detection and measurement of some metabolites; for example, DDA resulting from DDT and paranitrophenol from parathion. There are many other metabolites which at this point I'm sure that we don't know about. As in the case of DDT and heptachlor, they may be either less or equally or more toxic than the parent compound. Here, we are as concerned with identification as quantitation.

Finally, pesticide residue analyses are utilized to determine the decomposition of pesticide products. These methods have shown that many pesticide agents are decomposed by weathering such as rain, sunlight, wind, and temperature alternation. Such decomposition products may also be more or less dangerous than their parents. Once again, identification is more important than quantitation.

The final area within the "essential background information category" is a recognition of the type of analytical work we are faced with and some of the major problems we will encounter. First, we must consider the extremely large number of chemical species used as pesticide agents. These range from the extremely large volume of organic-chlorine compounds through phosphates, carbamates, thiocarbamates, into the oximes, substituted ureas, anilines, and many other chemical species. There is certainly no single method of analysis by which we can determine all of these species. We have methods which are useful in the analysis of organochlorine materials, those for organophosphates, for carbamates, and others. A few of these procedures may be utilized for one or two or perhaps a half dozen different chemical species. Generally speaking, however, we have methods which are useful only within one chemical species. In addition, degradation products, metabolites, and reactants will probably require still other methods.

Our samples are usually chemically complex. In the past and even today we consider that most pesticide compounds are primarily in the fatty portion of the media, and for the most part we are still isolating the fatty portion first and then separating the pesticides for analysis. We are finding that we should not be quite so concerned about getting the fatty portions out because there is considerable evidence that pesticide compounds are not associated merely with the fatty portions. We currently have more polar materials being used as pesticides and a host of polar metabolites and degradation products. These will not be found in fatty tissue.

As we know, the concentrations of pesticides are essentially trace quantities. Consequently, we find ourselves with an analytical problem which is somewhat worse than looking for a needle in the haystack.

We find that a given analytical procedure often is not applicable to different sample types. One of the procedures on which I worked some time ago, a simple saponification procedure, is very successful with just about any food product except corn oil. Corn oil, however, refuses to be saponified and continues to contaminate the detection system.

For many years now there has been a concerted effort to develop rapid procedures by which we hopefully could do the same job. Generally speaking, we can expect rapid procedures to result in somewhat less sensitivity than the more complex ones. Even more important, we know that the rapid procedures are not as specific. When we combine a rapid preparation procedure with a nonspecific detection system, we find ourselves in the hazardous position of potentially producing erroneous data. By such procedures, the insecticide aldrin is still being reported in human tissue, and we know that aldrin cannot possibly be in human tissue because it is metabolized to the epoxide, dieldrin. Also by these methods we have found that DDT has been reported in soil samples which were taken back before the advent of DDT. Thus, rapid procedures combined with nonspecific detection systems have in the past given us erroneous and undependable data.

We must also bear in mind that methods developed for a particular pesticide are usually not entirely specific. An example of this is the very excellent Schechter-Haller procedure for DDT. In this procedure, one must be extremely careful to remove any related materials consisting of benzene rings; otherwise, one will report DDT results which are higher than they actually exist in the sample.

Finally, we must keep in mind that all methods and equipment, like people, are fallible and we must determine and recognize their capabilities and shortcomings. Most of our popular instrumentation is not capable of both qualitative or quantitative analysis. Thus, we must frequently use confirmatory methods and instrumentation.

The second category, preparation for analysis, includes the requirements for the physical plant, equipment, and the analyst.

The physical plant does not have a great number of absolute requirements. Of course, you know that it needs a certain amount of benches, some sort of still, grinders, sample preparation tools, and should be arranged in a manner which will make the laboratory as efficient as possible. Each group in each residue laboratory has their own idea as to how they would like their laboratory arranged. To a certain extent this depends on personal preference, the type of sample, the volume of sample, and exactly what types of results, both qualitative and quantitative, is expected from this laboratory. I don't propose to consider any part of laboratory organization or arrangement. I do want to call to your attention, however, that any residue laboratory should be totally air conditioned, both as to temperature and humidity. Temperature control is certainly essential from the standpoint of stable operation of some of our modern sophisticated instruments. It also creates a more productive laboratory. Humidity control, on the other hand, is very helpful in maintaining modern instrumentation and is essential to an efficient operation where one is using physical separatory procedures utilizing absorbents or other highly hygroscopic reagents or equipment. Consequently, temperature and humidity control will enhance the operating efficiency of the laboratory. Proper ventilation is essential to the comfort and safety of laboratory personnel.

The equipment available in the residue laboratory should be sufficient to do any analysis required. Equipment should be selected both from the standpoint of qualitative and quantitative capability. When we consider chemical methods of analysis, we normally find that both qualitative and quantitative capability are included in the same method. More recently, since we have gone to a large extent to physical methods of analysis such as chromatography and spectroscopy, we often find ourselves in a position where dependable qualitative and quantitative work cannot be accomplished with the same tool. It is essential that we have equipment in our laboratory that will do both these jobs well. In addition to this, we have found ourselves more recently in a position of such sophistication that it seems like it is almost impossible for us to use any piece of equipment unless it costs a small fortune. Don't allow yourself to get into this position. Use whatever piece of equipment will do the job. Don't concern yourself with the fact that it may be inexpensive. In other words, keep in mind that the best tool for this particular job may not necessarily be the most expensive. Don't use a micrometer to measure your desk top.

Finally, the analyst is the key to the quality of the residue work. It is important that the analyst has a knowledge of the total picture. To this end, it is imperative that he spend considerable time with the literature. Literature reading without understanding, of course, is useless. Consequently, it is absolutely essential that residue analysts are familiar with the terminology used in that literature; the terminology used in pesticide residue work. For example, one must realize that a picogram is defined as 10^{-12} gram, a nanogram is 10^{-9} gram, and a microgram is 10^{-6} gram. We should recognize the designations for these fractional components of a gram, including the designation of Mmg used in the AOAC book of methods to represent a microgram. It is also necessary that we recognize that a microliter is one-millionth of a liter, or one one-thousandth of a milliliter and that it is referred to by many people as a lamda. These are only a very few examples of the terminology with which one must be familiar. One also must be familiar with the characteristics of solvents and the terminology used to define these characteristics. When instruments are utilized in the analytical scheme, the field of terminology becomes quite broad. Terms like wave lengths and reciprocal centimeters used in spectrophotometry, retention time, cell volume, partition, and many others found in chromatography, and the milicurie, half life, disintegration per minute, decay rate, beta and gamma emission, involved in the radioactivity utilized in detection cells, and method development, are terms important to the analyst.

Knowledge of the chemistry of each of the agents for which we are analyzing is essential to tne residue chemist. He must have a picture of the agent for which he is analyzing so that he will know the chemical elements involved in construction of this agent, the steric relationships or configurations of the molecule, and the reactive groups or weak links in the chain. With this knowledge, he will be able to predict the degradation products involved in the analysis of any given compound. He needs to know the methodology thoroughly. A residue analyst, or for that matter any other type of analyst, is not very well equipped if he simply follows a cookbook.

The analyst needs to know the capability of his equipment. He should know what to expect from this equipment and what the equipment will not accomplish for him. We will discuss the capability and use of equipment and methods in a few minutes.

The analyst must be both patient and determined. Almost all of our work is done with biological tissue and biological tissue is notoriously slow to react. Consequently, we must be determined to accomplish our analyses and patient in order not to force the method beyond its rate nor carry out the procedure or reaction in a hurried or haphazard manner.

The residue analyst must be completely attentive to all details in his method. Much difficulty has come about because of spur-of-moment modifications in the hope of shortening the procedure. This sort of problem is brought about simply because the analyst does not understand the methodology and doesn't pay enough attention to what is occuring during the procedure. Residue analysis, while we like to call it a science, certainly at this point is not exacting enough to be a pure science. It still reflects much of the art. Any good artist is extremely patient in his work, determined to accomplish what he wants and is exacting in every detail. The residue analyst is a hybrid; he is first a scientist, a trained chemist, and as a trained chemist should pay full attention to details. The other side of his hybrid character is that of the artist. Unfortunately, until methodology becomes completely, fully, and totally scientific, we still must also play the role of the artist.

The third requirement of the residue analyst is that of practice. So long as the analyst remains patient and determined and pays attention to details, the longer he practices, the better he will become. This is not peculiar to residue analysts since dedicated practice makes anyone better at his job. Bear in mind the term "dedicated practice"; there are those who can spend fifty years on the same job and in the final analysis that job is more poorly done than it was fifty years ago.

The analyst must have a strong interest in his work and will benefit considerably from any advanced training available to him. He must have the ability to reason and thus to be able to find solutions to problems which generally are in constant occurrence.

Above all else, the analyst must have a desire for personal improvement. "No person can stand still; he must move forward or he will slide backway" is a statement of fact as far as our work is concerned.

The final job that the analyst must do is to interpret the data which he has obtained. The qualitative interpretation of that data consists of being as sure as one needs to be that the compound reported is indeed the compound that is present. We will present a considerable amount of information to you on gas chromatography since that is unquestionably the method of choice for residue analysis. However, in the absence of a specific detector, qualitation on the gas chromatograph depends entirely on retention time. In certain instances it then may be necessary for the analyst to use other procedures to confirm the data obtained from the gas chromatograph. Thus, you must know your methods and equipment. The analyst should always realize that no instrument or analytical method is infallible and should be aware of the pitfalls in methodology where many amateur and even a few seasoned veterans have placed themselves in an embarrassing position. Quantitatively, we have somewhat less of a problem. However, we must ensure the accuracy of standard solutions, sample weight, extraction procedure, instrument calibration, and calculations.

Data interpretation requires a critical attitude towards the literature, the results, the methods, the equipment, your associates, and above all, yourself. We must recognize the relationships among pesticides, concentration ratios among tissues, and to a limited extent the effect of pesticides on tissues and the characteristics of pesticides which will influence the data obtained. Be suspicious of any unusual result and obtain as much information on the sample as possible to help you to explain such unusual results.

Keep in mind the potential problems associated with laboratory safety. Protect yourselves from human tissue samples. Recognize the expositive and flammable nature of organic solvents and their potential capability to asphixiate you in the absence of proper ventilation. Recognize the subtle intoxication potential of relatively safe solvents. Remember the explosive characteristic of reagents such as sodium, phosphorus, thionyl halides, and the corrosive action of acids and bases. Watch out for cuts, burns, and electrical shock from glassware and equipment. Finally, treat all radioactive materials with respect. Use protective clothing; use equipment responsibly, and follow good housekeeping and sanitation practices. Know the operation of your equipment. The inadvertent improper operation of laboratory equipment can lead to erroneous interpretation of results as well as breakdowns and extensive delays.

Maintenance of equipment is imperative. The analyst must budget time for maintenance. Proper maintenance will not only enhance the production of dependable data but will assist in maximum work output and the elimination of expensive repairs.

The recommendation or selection of methodology is often the responsibility of the analyst. In the event that methods are selected for you it still remains your responsibility to recommend any changes which you feel will improve your program. In order to be in this comfortable position, it is essential that you be familiar with your methods. This does not mean a cookbook familiarity. I am talking about the necessity for knowing wh y as well as what we are doing. In addition to placing you in a position of recommending changes, this knowledge will allow you to apply the method rapidly, interpret your data intelligently, and prevent the inherent desire to take hazardous shortcuts. Such knowledge will provide you with a professional as well as a physical safety factor.

We will now consider the last category, the actual analysis of the sample. There are a multitude of "wet chemical" methods for the preparation of samples of various media for analysis. We will first consider the methods available for analysis of extracts and reserve the sample preparation, extraction and cleanup for the last portion of our discussion.

Thin-layer chromatography is the first method to be considered. The principle of thin-layer chromatography is partition between a solvent and an adsorbent layered on a glass or plastic plate. This procedure is sensitive in the nanogram range. It is utilized as a qualitative and semi-quantitative procedure, following a very extensive cleanup. Thin-layer chromatography has two extensions of the procedure that should be mentioned. First, detection chemicals are often incorporated in the adsorbent layer for rapid identification. Colormetric determination by this procedure can be made directly on the plate by incorporating the proper chemical reagents into the adsorbent layer. Second, thin-layer chromatography has been used at times for additional cleanup of the sample extract where it is necessary to use other means of identification. We can isolate and concentrate the pesticide by thin-layer techniques.

The second group of methods are the biological procedures which we heard a great deal about a few years ago. We don't hear too much about them any more although some investigators are using these procedures to do a particular type of job. First, the bio-assay procedure. A great variety of organisms has been used as bio-assy subjects from micro-organisms to various types of fish. We have a rather large biological assay colony in the marine biological institute at the University of Miami.

These investigators are using fish colonies to monitor water for toxic compounds. Bioassay procedures have a long sample completion time; however, a large number of samples can be analyzed simultaneously. The only limitation to the number of samples we can assay at one time is the size of the biological colony. The bioassay colony requires very few man hours when one considers the number of assays which can be made over a given period of time. Biological assay has suffered from a number of criticisms in the past, the principal one being that too often the bioassay colony has been treated as a parttime job. It is a full-time job which requires a well-trained biologist as its director. In addition, the care of the organisms themselves is an added responsibility and expense which management sometimes cannot justify. There is, at times, considerable difficulty in the interpretation of the bioassay data. We occasionally have rather high blank values. Organisms may die for unknown reasons; sometimes we have a large mortality rate even among the controls, sometimes in the experimental subjects which upon detailed study appear to have absolutely nothing to do with the compound being analyzed. There is also an inherent variable sensitivity and lack of reproducibility. Assay organisms undoubtedly vary in their sensitivity and response to a particular agent in much the same manner as members of the human race. Bioassay procedures have many advantages. A large number of samples with few man hours of labor may be analyzed over a given period of time. It is also possible that the extensive cleanup, required for every other procedure may not be necessary for bioassay, depending on the medium. Biological assay can be used for any agent which will kill the assay organism. This procedure should be useful in screening large numbers of samples; however, since the response is general, confirming procedures would be required to define positive samples.

A second type of biological procedure which is being used in particular situations is enzyme inhibition. One procedure of this type constitutes a general analysis for cholinesterase inhibition by organophosphate and carbamate insecticides. This is almost a natural procedure as used on blood to determine the activity of the enzyme cholinesterase, normal to blood. Either phosphates or carbamates reduce the activity of the enzyme cholinesterase. If one can establish a base line for the activity of this enzyme in the blood, one can measure the reduction of activity as a result of these toxic agents. The same difficulties we discussed under bioassay exist here in that the sensitivity and reproducibility is rather variable, simply because we really don't have a constant base line for cholinesterase activity in the human organism. None the less, it is of value in this type of determination. There have been some attempts to use this with other samples, but as far as I'm aware, it has little if any utility.

The third, the old timer, is the group of chemical procedures. First, the colormetric procedures whose principle is that of forming a colored complex with a pesticide or decomposition product of a pesticide. The best example of this type of procedure is the Schechter-Haller procedure for DDT. There are many others; actually as I understand it there is a procedure for every pesticide registered for sale. I believe that this procedure is colormetric in nature or at least has been in the past. I have indicated the chemical colormetric procedure as being sensitive to microgram quantities; actually there are lesser quantities. As with the Schechter-Haller, and even more so in some cases, these procedures are all time consuming. Chemical procedures require more attention than chromatographic; consequently; few samples per man can be analyzed in a given period of time. As I indicated with the Schechter-Haller, they usually are not entirely specific even though they are so designed. Normally, a great deal of special laboratory equipment is not required; thus a chemical colormetric procedure, equipment wise, is an inexpensive procedure. Even though these procedures have been reported to be time consuming, there may be times when the use of a specific chemical colormetric procedure will be less expensive than one of the more general techniques. That is, more samples may be analyzed in a given period of time.

Chemical titrametric procedures are the second group of chemical procedures. The principle is the chemical comsumption of the pesticide or decomposition product of the pesticide by standard solutions. Probably the best known of this group of methods is the total chlorine procedure. As with other chemical procedures, total chlorine is rather time consuming although there have been modifications resulting in rather rapid determination of total chlorine. The results here, of course, are general because we simply consider all of the organochlorine containing compounds in one group and measure the total amount of chlorine. While this procedure may be useful in some applications, the type of work in which we are involved requires more information than would be provided since the results are general. It is sensitive to fractions of a microgram. Generally speaking, we do not require a great deal of additional equipment if any. Due to varying concentrations of organochlorine naturally occurring in the sample under analysis, we often find variable reproducibility and sometimes very high blank values resulting in extreme difficulty in the interpretation of results. We will mention an instrumental procedure in a moment which utilizes electrometric titration.

Gas chromatography is currently the preferred method for residue analysis, generally being used as gas-liquid chromatography. Chromatography is essentially a physical separation technique based on the principle of partitioning the components of a mixture between two or more phases. As used in pesticide residue analysis, the gas chromatograph consists of a glass column packed with an inert support material upon which is coated one or more silicone greases or oils, a supply of carrier gas which flows through the column, the appropriate temperature and gas flow controls, a suitable detection system, and a system for placing the sample on the column. The entire system is controlled at the appropriate temperature and the sample is forced through the column by the carrier gas, adsorbing and desorbing between the column material and the gas, in accordance with the partition coefficient for each component of the mixture. Since the partition coefficient of the components differ, we will achieve separation; the components will enter the detectors at different times; and each can be measured separately. We refer to the time required for a component to reach the detector as the retention time. Retention time is our means of identifying components on the gas chromatograph. On any given type of column we must remember that many components can have the same retention time. Thus, in the absence of a specific detector we must use other means of confirming the identity of what we think we have found. Ironically, the gas chromatograph, basically a separating tool, is not the best identifying equipment.

A number of detection systems have been used with gas chromatography, the most popular and most sensitive being the electron capture. The electron capture detector functions as follows:

1. Electrons are produced in the electron capture cell by the action of a radioactive source on the carrier gas, producing an electric current which is monitored and recorded.
2. Electronegative compounds will capture these electrons and thus show a decrease in the number being monitored, commensurate with the amount of the compound present in the detector at any given time.

Since the electron capture detector will respond to any electronegative compound, it is useful for a large number of pesticides. On the other hand, however, it is a selective but not a specific detector. Thus combined with the rather nonspecific retention time data, the electron capture detector frequently needs confirming analyses for identification of a given compound. The prime advantage of this detector is its extreme sensitivity, frequently as little as one picogram can be detected.

A second group of useful detectors are the electrochemical, microcoulometer system, and the electrolytic conductivity cell. Microcoulometry is essentially an electrometric titrating system which measures the pyrolized eluate from the gas chromatograph. Pyrolysis produces species which can be measured by silver titration in the silver cell, oxidation-reduction in the platinum cell, or pH change in the hydrogen cell. Microcoulometry, while not as sensitive as electron capture (5 ng of element), provides a more selective chemical response and when combined with retention times, offers an improved means of identification over the electron capture detector. This system also has the advantage of detecting and measuring sulfur and nitrogen as well as the halide elements.

The electrolytic conductivity cell utilizes pyrolysis and electrical conductance within a small volume cell to measure any water soluble gas such as halides and nitrogen. The sensitivity is about one ng of the elements. Specificity is somewhat less selective than the microcoulometric system.

The third useful detector is referred to as the flame photometric or melpar detector. This system functions by burning the sample extract in a hydrogen-rich flame and observing emissions of rather specific wavelengths. Thus far, the flame photometric detector has been used with excellent results for phosphorus, sulfur, and chromium down to 1-0.5 ng. This is an excellent identification tool since we can view the element at its specific wavelength emission.

The second type of instrumental system is the infrared spectrophotometer. This is primarily a qualitative instrument, quite contrary to the definition of the gas chromatograph. The infrared spectrometer can also be a quantitative tool, but unfortunately it lacks the desired sensitivity for pesticide residue work. Consequently, its primary function is that of a qualitative tool. For infrared work, we require an extensive cleanup of the sample since we are attempting to obtain a spectrum of only the material with which we are concerned. Any other substance in the sample will provide us great difficulty in the interpretation simply because the spectrum we obtain will be a combination of all materials present. Infrared spectroscopy requires rather well trained analysts. The infrared unit is not particularly difficult to operate nor is it any appreciable problem to maintain. The training of the analyst is required to interpret the data obtained.

Very good results are obtained by utilizing a combination of instruments such as gas chromatography for separation and quantitation and infrared spectroscopy of mass spectroscopy as the qualitative or identification tool. From the standpoint of qualitative work or identification, excellent results have been obtained with thin-layer chromatography-infrared combinations. We are apparently able to get much cleaner samples for the infrared by utilizing thin layer as the resolving, separating, concentrating, and additional cleanup step before infrared analysis.

Sample preparation procedures are almost endless in number.

Thus, we will consider a typical multiresidue procedure of both the cleanup and noncleanup types and an example of reaction procedures such as is used for metabolites, degradation products, and certain other pesticide compounds. Bear in mind that modifications of these procedures may be necessary for different types of media.

The most famous and useful cleanup procedure for multiresidue, both organochlorine and organophosphate, is that developed by Mills, Onley, and Gaither of the Food and Drug Administration. Samples are thrice extracted with either petroleum ether or hexane to remove the residues. These solvents also remove fats and oils, waxes, and other undesirable materials such as carotenoids and various steroids. Since all of these contaminants have been found to interfere in subsequent analytical steps, we remove the fatty materials by liquid-liquid extraction with acetonitrile and the remaining contaminants on a florisil adsorption column. The concentrated extract can usually be analyzed by the equipment previously discussed.

Non-cleanup procedures, generally, simply extract the sample with the appropriate solvent and analyze without further treatment. Such procedures usually produce undependable quantitative data and always result in a short life span of the determinative instrumentation. Such extracts can be used only for tentative identification and are certainly not recommended for any analysis.

A considerable number of reaction methods are available such as the procedures for DDA, pentachlorophenol, and other pesticide phenolics, alkyl phosphate metabolites from organophosphates, and many others. All of these procedures have a common denominator, that of preparing a derivative which can be analyzed by our instrumental procedures or a derivative which will increase the detection sensitivity. References to the methods are supplied for your use.

In summary, the residue analyst is called upon to cover the area from a plumber to a literature scientist. He must know as much as possible about the characteristics of pesticides, solvents, and reagents. He should be familiar with the known effects of pesticides on the human animal. He must be familiar with his methodology and know how to select, setup, maintain, and operate analytical equipment, and the requirements for dependable data interpretation.

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PESTICIDES IN FOOD AND FEED

L. L. Ramsey

Perhaps, it would be illuminating to look at major historical developments to see how we arrived at this point in pesticide regulation and then to conclude with a review of FDA's pesticide residue findings in food.

1906 - The Food and Drugs Act of 1906

The administration of this Act was lodged in the old Bureau of Chemistry of the U. S. Department of Agriculture. The Act contained no authority for establishing pesticide residue tolerances.

The Act required the Government to "establish that the added poisonous or deleterious substance may render the article injurious" before it could take action against a shipment of food bearing excessive pesticide residues.

1910 - Federal Insecticides Act of 1910

This Act covered only insecticides and fungicides and was intended to protect the farmer against adulterated and fraudulent products.

1927 - The regulatory functions of the Bureau of Chemistry were separated from the research functions and the Food, Drug, and Insecticide Administration was created to administer the Food and Drugs Act of 1906 and the Federal Insecticides Act of 1910.

1920 - 1939 - A period of zealous regulatory action against shipments of fruits and vegetables containing excessive residues of lead, arsenic, and fluoride, particularly during the 30's. The informal tolerances for spray residues on fresh fruits and vegetables had been reduced yearly until in 1932 they were set for arsenic at 1.4 ppm; lead, 3.5 ppm; fluoride, 2.8 ppm.

1938 - The Federal Food, Drug, and Cosmetic Act enacted

This Act contained the so-called poison *per se* rule: "Any poisonous or deleterious substance added to any food except where such substance is required in the production thereof .... shall be deemed to be unsafe ...." The law also provided authority for establishing safe tolerances for poisonous substances such as pesticides.

1940 - President Roosevelt's Reorganization Plan

The Food and Drug Administration was removed from the Department of Agriculture and placed in the new Federal Security Agency. The unit administering the Insecticides Act was left in the Department of Agriculture.

1940 - Informal tolerances on apples and pears were raised after a study by the Public Health Service as follows: arsenic, 3.5 ppm; lead, 7 ppm.

1944 - First legal tolerance established for a pesticide residue at 7 milligrams fluorine per kilogram on apples and pears.

1945 - Informal tolerance for DDT set at 7 ppm on apples and pears.

1946 - Court decision held the tolerance for fluorine to be null and void because the residue was actually cryolite, not fluorine.

1947 - The Federal Insecticide, Fungicide, and Rodenticide Act was enacted

This Act was designed to exercise more effective control over pesticides, particularly the new organic pesticides which were proliferating. The Act requires label registration of these pesticides moving in interstate commerce, the registration being based upon data showing that the pesticide is effective for the control of pests and safe when used in accordance with directions on the label.

1950 - The Delaney Committee hearings on pesticides and food additives.

1950 - FDA spray residue hearings with respect to fresh fruits and vegetables.

1954 - The Pesticide Chemicals Amendment (The Miller Amendment)

Established the present petition clearance procedure for setting tolerances for pesticide residues on raw agricultural commodities. This was the first pre-testing, pre-clearance procedure for chemical agents used on food. It shifted the burden of proof. The industry was required to show that the pesticide was safe before it was used instead of the Government being required to show that the pesticide was unsafe after it had been used.

1955 - Tolerances on fresh fruits and vegetables established for a long list of pesticides based on the 1950 spray residue hearings.

March 25, 1955 - Tolerances for residues of sesone established at 6 ppm on potatoes, peanuts, peanut hulls, peanut hay and at 2 ppm on asparagus and strawberries, the first tolerances under the Miller Amendment. Additional tolerances for other pesticides have followed to date.

1962 - Silent Spring by Rachel Carson contributed greatly to a general public awareness of the pesticide problem.

1963 - A Science Advisory Committee appointed by President Kennedy largely because of the furor created by Silent Spring issued a report entitled "The Use of Pesticides." The Committee recommended among other things that the concepts of zero tolerance and no-residue be reviewed, that the accretion of pesticide residues in the environment be reduced by orderly means, and that the elimination of persistent pesticides should be the goal.

1963 - Minute residues found in a wide variety of products because of the use of analytical methods based on gas liquid chromatography which have a sensitivity several magnitudes greater than the sensitivity of methods previously employed and provide means of finding metabolic products. Extensive regulatory action was taken against milk; cauliflower; dairy feed, such as alfalfa, corn silage, and dried sugar beet pulp; and other food crops.

October 13, 1963 - The actionable level for DDT residues in milk was reduced from 0.1 ppm to 0.05 ppm for DDT and for dieldrin and heptachlor epoxide it was set at 0.01 ppm and the states were notified.

May 1, 1964 - Interdepartmental Agreement

An agreement entered into voluntarily by the Departments of Agriculture, Health, Education, and Welfare, and Interior for the purpose of coordinating the activities of the three Departments pertaining to pesticides. This Agreement implemented one of the recommendations of the PSAC report of May 15, 1963.

April 13, 1966 - USDA and HEW published a joint statement of implementation of the report of an NAS-NRC "zero committee." Where there was any reasonable expectation of residue, however minute, the USDA would not grant a pesticide registration until the Food and Drug Administration had established a pesticide residue tolerance. The rather formidable task of converting a large number of label registrations by USDA based on no residue to label registrations based on a negligible residue tolerance got under way and still continues.

1967 - Tolerance established at 0.05 ppm for residues of DDT, TDE, and DDE singly or in combination in fluid milk pursuant to a report of a Scientific Advisory Committee dated October 26, 1966.

1968 - DDT tolerances lowered to levels no higher than necessary to cover residues incurred in good agricultural practice.

1969 - Tolerances for other pesticides reduced or proposed for reduction including captan, folpet, and TDE. Seizures of Coho salmon because of high levels of DDT.

In addition to the PSAC report of 1963, to which I alluded a few moments ago, there have been a number of other reports by nationally recognized advisory bodies. These reports are all directed toward a sound national policy on pesticides, and thus worthy of our consideration.

1. Ribicoff Report of July 21, 1966.

Senator Ribicoff served as the chairman of Senate Subcommittee.

The Report of this Subcommittee is well balanced. It recognizes the valuable role the newer chemical pesticides have played in the improvement of agricultural production and in the furtherance of public health and it recognizes the dangers to our overall environment as suggested in Miss Carson's popular book Silent Spring. In a section headed "The Benefit-Risk Equation" it is stated that "the committee found no reliable evidence to suggest that the benefit-risk equation was presently unbalanced in any significant way." However, the Report goes on to warn that more information is needed to guarantee future balance of the benefit-risk equation and to assure public confidence. This Report included a comprehensive series of recommendations.

2. Whitten Report, 1966.

Congressman Whitten served as the Chairman of a Subcommittee of the House. This report notes that the book Silent Spring by Rachel Carson influenced the concern of the public over the use of pesticides and points out the unwarranted implications in this book. In general, the report is not critical of the use of pesticides; no recommendations were made.

3. The NAS-NRC Report on Persistent Pesticides, May 1969.

In the preface the Committee refers to the PSAC Report of 1963 and notes that progress has been made but expresses concern about what remains to be done and about gaps in knowledge of pesticides. The Committee declares ".... there is an immediate need for world-wide attention to the problem of buildup of persistent pesticides in the total environment."

The principal recommendation of the report is "that further and more effective steps be taken to reduce the needless or inadvertent release of persistent pesticides into the environment."

4. HEW Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health, November 1969.

November 1969 - HEW Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health.

While the Commission found itself in agreement with this rather broad and general recommendation of the NAS-NRC Committee on Persistent Pesticides, it concluded that the value of this recommendation would be considerably enhanced if it were made somewhat more specific and spelled out in greater detail. Toward this end, the Commission directed a number of specific recommendations carefully weighing the benefits of modern pesticide usage against the possible risks to man's health and the quality of his environment. In all, the Commission made 14 specific recommendations, but I believe that only three are of sufficient interest to this audience to be mentioned at this time.

III. Eliminate within two years all uses of DDT and DDD in the United States, excepting those uses essential to the preservation of human health and welfare and approved unanimously by the Secretaries of the Departments of HEW, Agriculture, and Interior.

IV. Restrict the usage of certain persistent pesticides in the United States to specific essential uses which create no known hazard to human health or to the quality of the environment and which are unanimously approved by the Secretaries of the Departments of HEW, Agriculture, and Interior.

V. Minimize human exposure to those pesticides considered to present a potential health hazard to man.

Besides these there have also been the reports of congressional hearings on specific aspects of our pesticide problem, such as the Fountain Committee hearings; all of these have exerted an influence on the pesticide policy of the Federal Government.

On December 2, 1970 the President's Reorganization Plan No. 3 became effective. This plan created the Environmental Protection Agency and transferred the responsibility for establishing tolerances for pesticide residues on raw agricultural commodities and processed food from the FDA to the new agency. FDA will continue with its pesticide tolerance enforcement program as well as its monitoring program for pesticide residues in food.

In conclusion, our over-all basic problem in the pesticide area is to decide what actions should be taken consistent with a policy that will keep the benefit-risk equation in balance, because the safety of any pesticide usage is not absolute regardless of the quantity of favorable data that may have been adduced. There is always some risk, be it ever so slight, and thus the benefits that may accrue from the usage of any pesticide must be weighed against the risk to be incurred.

Attached is Dr. Duggan's paper entitled "Regulatory Control of Pesticide Residues in Foods."

REGULATORY CONTROL OF PESTICIDE RESIDUES IN FOODS

By

R. E. DUGGAN[1] and G. Q. LIPSCOMB[2]

Even though the subject is not new, the regulatory control of pesticide chemicals has been receiving increased scientific and public attention as a part of the increasing awareness of the larger problem of environmental pollution.

The emotions and instincts of society come into the picture with real or imagined threats to survival. The presence of toxic substances - pesticides, bacteria, mycotoxins - in the food supply poses an implied threat to survival. In this context, action to reduce the threat is inevitable under our system of government. This is particularly applicable where the individual has little direct knowledge and consequently little freedom of choice. As a result, control systems are developed in his interests.

A rather complex system of laws, regulations and rules govern the use and control of pesticide chemicals in the United States and involve the U. S. Department of Agriculture, Department of Health, Education, and Welfare, and the U. S. Department of Interior.

The purpose of the system is to insure the safe and effective use of pesticides. The system undergoes continuing change to better serve this purpose by reflecting the advances in scientific knowledge. There have been several comprehensive reviews of pesticide residues in foods (1)(2)(3) indicating that notable increases in levels of residues had not been observed through 1967. Reports (4)(5) have been made on the dietary intake of pesticides as measured by the Food and Drug Administration's market basket survey on data obtained through April 1968.

This report includes summary data obtained from the Food and Drug Administration's surveillance program through June 1969, and from the market basket survey through April 1969. These programs have been described in detail(6).

A brief description of that portion of the FDA control activities which has been the source of the data used in this report may assist a better understanding of the significance of the findings. One objective of the program is to improve the surveillance system to detect the lots containing excessive residues and keep them from entering food channels. Another objective is to maintain surveillance adequate to detect changes that may be taking place within sanctioned levels so that corrective measures may be applied before a problem arises.

First, surveillance activities determine compliance with tolerances and sanctioned uses and include inspectional investigations in the growing fields and the analysis of pre- and post-harvest samples. Second, information and education activities keep the grower knowledgeable of our findings, good and bad. This is to assist the grower in avoiding shipment of foods with illegal residues. Third, there are regulatory activities to remove hazardous foods from consumption channels through State and Federal legal actions. Finally, there are the total diet studies which are used as an index to the dietary intake of pesticide residues, which is where the hazard lies, and serve as the final check on the effectiveness of the control system.

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During the past six years, the Food and Drug Administration has examined 95,736 objective samples of foods from lots shipped in interstate commerce. Table 1 shows that pesticide residues of one kind or another were found in slightly more than half of the samples and that about 1/3 of these samples contain residues of more than one chemical. Even though residues are widely distributed and commonly found in foods, the levels are relatively low. For example, during the six year period, 75-80% of the individual residues were below 0.11 ppm and 95% were below 0.51 ppm.

Inspection of this table indicates there has not been significant change in the incidence of residues in the general food supply. Although many different pesticide chemicals are identified each year, relatively few are found at an incidence rate of 1%. The high incidence of residues on foods is not unexpected since there are over 201 pesticide chemicals which may be used in the production of food crops and over 3,383 tolerances for residues in food have been established.

There is general compliance with tolerances or with administrative guidelines in the absence of tolerances. The incidence of residues exceeding these sanctioned levels ranged between 2.3 percent and 3.6 percent during fiscal years 1964-1967, inclusive. There is, of course, a much wider spread in the incidence of illegal residues within food categories or individual foods. There have been a number of instances during the past several years where substantial quantities of food contained excessive residues. In most cases, investigations revealed a misuse of the pesticide chemicals. The term administrative guideline is not well understood. FDA administrative guidelines and FDA tolerances are not interchangeable terms. They do not have the same meaning nor are they used for the same purpose. Tolerances are established through procedures requiring a showing of safety and a need for use. When a tolerance is established, theoretically at any rate, it is applicable to all lots of the food for which it is established and safe to consume at that level. In actual practice, the tolerance level is not expected to be found on all lots of food. This expectation is borne out by experience. Guidelines are set where there are no tolerances and where there is a need for general limiting values in the absence of specific information concerning the source or cause of the contamination. Generally, they are high enough to allow for unavoidable or indirect contamination and low enough to detect purposeful or direct uses. These guideline levels must also be safe levels. Again, it is not expected that all lots of food contain the guideline levels and experience bears out this expectation. Guidelines are not applicable when there are instances of misuse or deliberate unauthorized application. Guidelines, and tolerances for that matter, are subject to change as additional information becomes available. As negligible residues are established in place of "zero" tolerances and "no residue" registrations (7), the need for administrative guidelines will not be as great. The comprehensive report "Pesticides and Their Relationship to Environmental Health," (8) and recommendations to the Secretary of the Department of Health, Education, and Welfare will probably result in actions to lessen the need for administrative guidelines.

Findings on surveillance-type samples are normally reported to the grower or shipper to partially fulfill the second activity. If the levels are below tolerances or guidelines, as all but a low percentage are, the report serves only to reassure the grower or shipper. If the results are above sanctioned levels, the grower may take some action to reduce the levels, as postponing harvest date, washing or other steps to insure that no lots with illegal residues enter food distribution channels. Inspectional observations are also reported to growers or shippers as a positive approach to resolving the basic practice which is resulting in illegal residues.

The third activity is quite simple in nature and very effective. When necessary, seizure actions are taken on lots containing illegal residues.

The final check on the control system is the measurement of levels of pesticides on foods as consumed. Obviously, there are reductions in residue levels during food preparation processes.

Investigations (9)(10)(11)(12)(13) have been made on the effect of home and commercial preparation and cooking on the pesticide residue content of certain vegetables.

Although there is no direct relationship between the thousands of surveillance samples of raw foods and the 134 market basket samples, a general comparison of the residue levels is of interest. One such comparison is that between the average level of DDT calculated from all samples in several major food classes with that calculated from the same food class in the total diet samples. This is shown in Table 2.

The approximately 120 food items in the total diet study are separated into 12 similar classes of food such as: dairy products; meat, fish and poultry; root vegetables; legume vegetables, in order to obtain more valid analytical results and to minimize the dilution factor. Dairy products are included in this tabulation to show the relation between the two programs.

There are no significant processing changes in the composition of fat of dairy products from the objective samples to the total diet samples. Thus, a comparison of the two sets of values is permissible using dairy products as a check point.

Another comparison is that between the averages calculated for the most commonly found pesticide chemicals from the dairy products composite of the total diet samples and from the surveillance samples of fluid milk and dairy products. These results are shown in Table 3. The results of both investigations are reported on a fat basis and since processing techniques used in manufacturing dairy products probably do not affect the pesticide residue content of the fat, each should serve as a check on the reliability of the results. There is remarkably good agreement between the two sets of values. Distribution of pesticide residues in the diet by chemical classes of pesticides is shown in Chart 1. The majority, 70-85%, of the dietary intake is of chlorinated insecticides, followed by organic phosphates, ranging from 5-20% with relatively little contribution, 5-10%, from carbamates and less than 5% of herbicides.

Table 4 shows the average dietary intake in milligrams per day calculated from the total diet samples of the 15 most commonly found pesticide chemicals. There has been no change in the order of magnitude of these values during the period 1964-1969.

The dietary source of the residues is of interest. Using the chlorinated insecticides as an example, residues in milk and dairy products form about 1/5 of the dietary intake. Residues in meat, fish, poultry and eggs account for about 1/4 of the dietary intake of this class of pesticide chemicals. These food classes make up about 25% of the diet used in these studies and account for almost half of the total intake of chlorinated pesticides.

The Food and Agricultural Organization of the United Nations and World Health Organization Expert Committee on Pesticide Residues (14) have proposed acceptable daily intake (ADI) values for some pesticide chemicals. The FAO-WHO Expert Committee has defined acceptable daily intake as "the daily dosage of a chemical which, during an entire lifetime, appears to be without appreciable risk on the basis of all facts known at the time. 'Without appreciable risk' is taken to mean the practical certainty that injury will not result even after a lifetime of exposure."

Table 5 compares the FAO-WHO acceptable daily intake level with the averages of those chemicals commonly found in the total diet samples. This diet was constructed as a well-balanced food supply for a 16-19 year old male. The food consumption is almost twice that of the normal person. No ADI has been exceeded during the five years of the total diet study, nor have all chemicals for which ADI's are proposed been found in the total diet samples. The calculated daily dietary intake of practically all specific pesticide chemicals is an order of magnitude (1/10) or more below that considered safe by the FAO-WHO scientists. At the 1969 meeting of the FAO-WHO Committee, the ADI for DDT compounds was changed from 0.01 mg/kg body weight/day to 0.005 mg/kg/day. This lower ADI has not been approached during the five years of the study. The dietary intake of pesticides, as measured by this investigation, shows that the tolerance and control system for pesticides in the United States is effective in assuring safe foods. The levels of residues found on raw agricultural crops are generally much lower than the tolerance, which has a built-in safety factor. These lower levels are expected because the tolerance must recognize the maximum residues resulting from safe and effective use of the pesticide under varying agricultural practices and conditions. Further, the levels of residues on the dinner plate are much lower than the legal tolerance level and, if the system is working properly, they will be lower than the ADI. Pesticide levels in foods are not constant. Instead, they are constantly changing. There have been, and continue to be, instances which could have resulted in significant increases in the dietary intake of pesticides. Fortunately, most were detected in the early stages and corrective measures taken before the problem became a national concern.

Foods of animal origin continue to be the major source of chlorinated pesticide residues in the diet. These residues, for the most part, do not result from sanctioned or direct uses of the pesticides. They result from environmental and indirect exposure. The dietary intake of aldrin-dieldrin, primarily from these sources are, for practical purposes, equivalent to the ADI. Even though the balanced diet used in this study is about twice that normally consumed, the significance of the observation is that the levels are approaching the ADI. It is conceivable that this ADI could be exceeded under certain dietary patterns. Restrictions in use of aldrin and dieldrin over the past several years apparently have been effective since there has not been any increase in the dietary intake in the U.S. during the past three years.

It is significant that there are at least 15 pesticide chemicals normally present in measurable amounts in food ready for consumption in the total dietary pesticide intake. Very probably, there are others which are not being measured because current analytical methods just do not measure all of the pesticide chemicals in all of the foods.

The annual production of synthetic pesticide chemicals exceeds a billion pounds, which means that burden in the environment as a whole, of which food is a part, is being increased by 20-25% annually from 1965 through 1967 (15). The preliminary figures show only a 7% increase in 1968.

An increased burden in the food supply is not yet observable from preliminary inspection of the data collected in the FDA programs. A more sophisticated analysis of this data is underway. The control system isn't overloaded yet, but at some point in time, there will be a saturation point with the inevitable result.

It will take the continuing combined efforts of the agricultural and chemical industries, the universities and the regulatory agencies, State and Federal, just to keep even. The early signals, such as shifts to higher levels in the proportion of residues currently at the lower levels in raw products, must be recognized. The movement of pesticides into foods from indirect sources must be limited because this movement is adding significantly to the dietary intake. Well-reasoned and deliberate action must be taken, however unpalatable, based on sound scientific evidence to maintain the existing safe levels in foods, as well as other environmental substrates.

TABLE 1

FREQUENCY OF RESIDUES IN DOMESTIC FOOD SAMPLES

	FISCAL YEAR						DOMESTIC & IMPORTS
	1964	1965	1966	1967	1968	1969	1970
SAMPLES EXAMINED	20,088	14,462	14,806	19,870	15,991	10,519	10,359
PERCENT WITH RESIDUES	44.3	53.6	52.6	57.2	55.0	57.6	68.1
PERCENT WITH MULTIPLE RESIDUES	23.8	33.3	32.8	36.0	34.1	*	-
NO. DIFFERENT CHEMICALS	(	81	)	76	83	57	64

*Data not available for FY 69

TABLE 2

DDT RESIDUE LEVELS
IN RAW AND READY-TO-EAT FOODS

(1964-1969)

		PARTS PER MILLION	
		OBJECTIVE SAMPLES	TOTAL DIET SAMPLES
LARGE FRUITS	Average	0.10	0.008
	Range	(0.02-0.25)	(0.006-0.012)
GRAINS AND CEREALS	Average	0.02	0.005
	Range	(<0.005-0.04)	(0.003-0.008)
LEAF AND STEM VEGETABLES	Average	0.14	0.013
	Range	(0.08-0.18)	(0.007-0.016)
ROOT VEGETABLES	Average	0.04	0.003
	Range	(0.03-0.04)	(<0.001-0.007)
DAIRY PRODUCTS	Average	0.03	0.033
	Range	(0.01-0.04)	(0.023-0.038)

TABLE 3

AVERAGE LEVELS OF PESTICIDE CHEMICALS IN DAIRY PRODUCTS
PARTS PER MILLION (FAT BASIS)

	Objective Samples				Total Diet Samples			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
DDE	0.066	0.087	0.069	0.058	0.074	0.050	0.063	0.048
Dieldrin	0.042	0.017	0.011	0.008	0.016	0.019	0.012	0.019
DDT	0.042	0.033	0.014	0.009	0.037	0.032	0.030	0.023
Heptachlor Epoxide	0.036	0.005	0.003	0.005	0.010	0.006	0.012	0.012
TDE	0.026	0.017	0.011	0.007	0.013	0.022	0.019	0.010
BHC	0.007	0.018	0.006	0.013	0.008	0.011	0.021	0.007
Lindane	0.004	0.006	0.001	0.001	0.005	0.003	T	0.001
Aldrin	0.001	0.001	0.001	T	0.001	0.001	-	-
Heptachlor	0.002	T	T	T	-	0.001	-	T
Methoxychlor	0.001	0.001	0.002	0.005	0.002	0.005	0.004	-

T = less than 0.001 ppm

(1) Average findings for Fiscal Years 1964, 1965 and 1966
(2) Average findings for Fiscal Year 1967
(3) Average findings for Fiscal Year 1968
(4) Average findings for Fiscal Year 1969
(5) Total Diet Samples June 1964 - April 1966
(6) Total Diet Samples June 1966 - April 1967
(7) Total Diet Samples June 1967 - April 1968
(8) Total Diet Samples June 1968 - April 1969

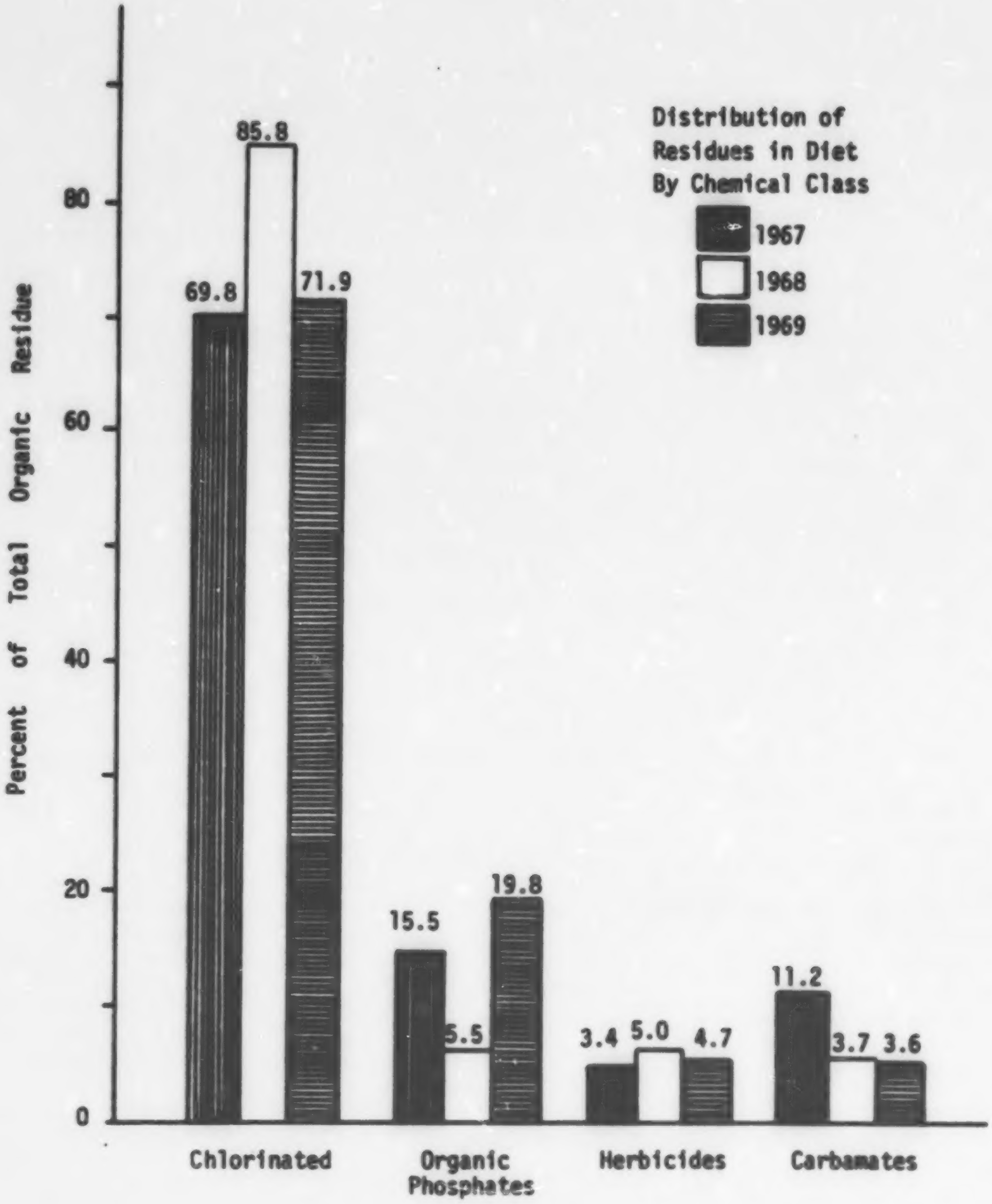
Distribution of
Residues in Diet
By Chemical Class
1967
1968
1969
Percent of Total Organic Residue
0
20
40
60
80
69.8
85.8
71.9
15.5
5.5
19.8
3.4
5.0
4.7
11.2
3.7
3.6
Chlorinated
Organic Phosphates
Herbicides
Carbamates

TABLE 4

AVERAGE DAILY DIETARY INTAKE OF 15 PESTICIDE CHEMICALS IN MILLIGRAMS

1965-1969

	Average	Range
DDT	0.027	(0.016 - 0.041)
DDE	0.018	(0.011 - 0.028)
TDE	0.012	(0.005 - 0.018)
Dieldrin	0.005	(0.004 - 0.007)
Lindane	0.003	(0.001 - 0.005)
Heptachlor Epoxide	0.002	(0.001 - 0.003)
BHC	0.002	(0.001 - 0.004)
Malathion	0.007	(0.003 - 0.012)
Carbaryl	0.037	(None - 0.150)
Aldrin	0.001	(<0.001 - 0.002)
2,4-D	0.002	(<0.001 - 0.005)
Diazinon	<0.001	(<0.001 - 0.001)
Kelthane	0.007	(0.002 - 0.012)
PCP	0.002	(<0.001 - 0.006)
Endrin	<0.001	(<0.001 - 0.001)

TABLE 5

DIETARY INTAKE OF PESTICIDE CHEMICALS

Milligrams/Kilogram Body Weight/Day

	WHO-FAO Acceptable Daily Intake	Average 1965-1969	Range
Aldrin-Dieldrin	0.0001	0.00008	(0.00006-0.0001)
Carbaryl	0.02	0.0005	(None-0.002)
DDT, DDE, TDE	0.01 (0.005)*	0.0008	(0.0005-0.0010)
Lindane	0.0125	0.00005	(0.00002-0.00007)
Heptachlor-Heptachlor Epoxide	0.0005	0.00003	(0.00002-0.00005)
Malathion	0.02	0.0001	(0.0001-0.0004)
Parathion	0.005	0.00001	(0.000001-0.00001)
Diazinon	0.002	0.00001	(0.000001-0.00002)
All Chlorinated Organics		0.001	(0.0008-0.002)
All Organo-Phosphates		0.0002	(0.00007-0.0003)
All Herbicides		0.0001	(0.00005-0.0001)

*Current Value Accepted 1969 Meeting

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Estuarine Pesticide Research—Bureau of Commercial Fisheries[1]

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Abstract

Pesticides that enter the estuarine environment can be accumulated by the fishery organisms that inhabit these fertile waters. Effects of pesticides on estuarine organisms and the fate of these chemicals in the estuarine environment are being studied at the Bureau of Commercial Fisheries (BCF) Pesticide Field Station, Gulf Breeze, Florida. Bioassay projects investigate the toxicity of new pesticides submitted by pesticide manufacturers and perform analyses requested by the Pesticide Review Board. Emphasis is placed on determining possible adverse effects of prolonged exposure (chronic studies) of fishery organisms to sublethal concentrations of selected pesticides. Ecological studies include the effect of a herbicide, Dichlohenil, on the ecology of an experimental pond. Experiments also are conducted to determine effects of sublethal levels of pesticides on the behavior of estuarine fish. For example, the capacity of fish to avoid water containing pesticides is tested in a special apparatus in the laboratory.

INTRODUCTION

The Bureau of Commercial Fisheries is vitally concerned about the harmful effects pesticides can have on estuarine organisms. Results of laboratory experiments on acute toxicity of pesticides to these organisms and other data indicate that residues of persistent pesticides are concentrated in the estuarine food web and may become toxic to predatory organisms. The evidence is clear that even low levels of pesticides (below those that cause mortality) can adversely affect the animals. In addition, commercial species are affected indirectly when their food organisms are killed or diverted to another habitat because of exposure to pesticides. This report discusses briefly the transport of pesticides to and within the estuarine environment and the Bureau's current research program to evaluate the effects of pesticides on estuarine fishery resources.

Pesticides can be classified according to their chemical structure or in reference to the animal or plant group which they are intended to control. Chlorinated hydrocarbon insecticides include such well-known chemicals as DDT and the aldrin-toxaphene group. These are persistent in water and sediments. Organophosphorous insecticides are much less persistent than the hydrocarbons and are degraded more rapidly in the environment. For this reason, they are usually preferred as control agents. Herbicides, such as 2,4-D, are now used in streams to control water hyacinths and are entering estuarine waters. Until 1964 more insecticides were sold than herbicides; but since then, sales in herbicides have taken the lead. Herbicides are generally less toxic to estuarine organisms than are insecticides.

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[1] Contribution No. 100

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Pesticides found in the estuarine environment originate from three main sources: agricultural applications, applications to control noxious insects and effluents from industries that formulate pesticides. Often, pesticides applied to an agricultural crop to enhance food production reach the estuarine environment through "runoff" and erosion. Many tons of pesticides are applied on a world basis annually and more will be required if food production is to be increased. This increase in tonnage could have a profound effect upon many forms of life other than the target pest—for example, mortalities or such subtle effects as lowered rates of growth and reproduction in clams, oysters, crabs and fish. Pesticides used to control mosquitos, stable flies and other noxious insects reach and affect estuarine animals in a similar manner. Oysters in Santa Rosa Sound accumulated DDT that was used to control larvae of stable flies found in dead sea weed on the beach (Butler, 1968). Pesticides released from industrial manufacturers can cause isolated instances of gross pollution.

Pesticides can reach the estuarine environment through movement of waterborne materials, direct application and aerial transport. Undoubtedly, water transports most of the pesticides that enter estuaries. Water draining from fields treated with pesticides carries these chemicals in solution and attached to silt into streams and rivers that eventually flow into an estuary. Most chlorinated hydrocarbons are only slightly soluble in water but adsorb readily to suspended material such as silt particles and organic detritus. These suspended materials often flocculate when they enter the saline environment in an estuary and become part of the bottom sediment. Pelagic animals may eat pesticide-laden detritus or food organisms and transport the pesticide to other parts of the environment. Pesticides sprayed directly into estuarine areas to control noxious insects and plants create relatively high concentrations of the chemicals in the water. Aerial transport is probably the least effective mechanism for introducing pesticides in estuaries.

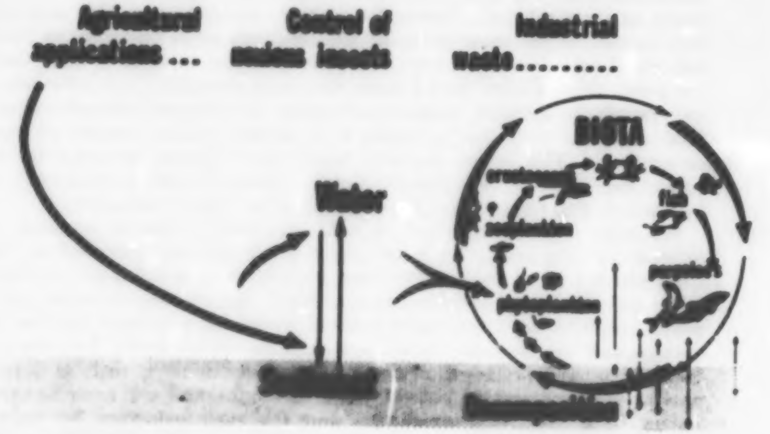
Agricultural applications ...
Control of noxious insects
Industrial waste.........
BIOTA
crustacea
fish
zooplankton
Water
predators
phytoplankton
Sediment
Decomposition

FIG. 1. Pesticides entering estuaries can become associated with water, sediment and biota.

In the estuary, pesticides become associated with one or more of three phases: water, sediment and biota (Fig. 1). Usually these chemicals are partitioned among all three phases, but accumulation by the biota is of particular interest. Organisms can obtain pesticides from the water and sediment. For example, phytoplankton can take up and concentrate pesticides directly from sea water. The pesticide is then transferred through the food web of the estuary. Residues of DDT in the sediment and organisms of a brackish marsh showed an increase in residues from phytoplankton to fish-eating birds (Woodwell, Wurster and Isaacson, 1967). Accumulation of DDT from organic detritus by fiddler crabs in a salt marsh was demonstrated by Odum, Woodwell and Wurster (1969). The particles of detritus contained residues thousands of times greater than the water, and crabs exposed to this material in the laboratory suffered loss of equilibrium. Other documentation of pesticides in estuaries is presented by Gray (1969). Thus, the potentially harmful effects of pesticides on estuarine fisheries is evident.

The Bureau of Commercial Fisheries began a research and monitoring program in 1958 at Gulf Breeze, Florida, to study the effects of pesticides on estuarine animals in the laboratory and to determine levels of polychlorinated pesticides in these agimals in many of the nation's estuaries. Much information has been obtained on the relative toxicity of various insecticides to clams, fish, oysters, shrimp and other estuarine animals. Presently, investigators conduct pesticide research in three areas: bioassay, ecological studies and physiological studies. Also, we participate in a nationwide monitoring program.

BIOASSAY

As new pesticides are developed for commercial use, there is a need for determining acute and chronic toxicity of these chemicals to estuarine organisms. In addition to conducting routine acute tests, we have recently devoted much effort to long-term bioassays involving the chronic exposure of selected estuarine species to low-level pesticide pollution.

The acute toxic effects of various insecticides on shrimp, fish, oysters and other estuarine organisms have been evaluated in the laboratory. These short-term bioassays do not provide conclusive data, but they do provide information on relative toxicity. Table 1 shows an example of some recent tests. As a group, insecticides were generally more toxic to all organisms than the other pesticides but there are exceptions. The fungicide, Delan, and the experimental antifouling agent, ET-546, were extremely toxic to oysters. Results of these and other bioassay tests are sent to the Pesticide Registration Division of the U. S. Department of Agriculture to assist in certifying pesticides to be used in or near the coastal environment.

The necessity for long-term or chronic tests on the effects of sublethal concentrations of pesticides was clearly demonstrated in the results of two experiments reported by Lowe (1970). Oysters (*Crassostrea virginica*) exposed to a mixture of DDT, toxaphene and parathion continuously for 9 months weighed less than control oysters after 6 weeks but did not show a statistically significant difference until the 22nd week. In another experiment, mortalities in blue crabs *(Callinectes sapidus)* due to mirex adsorbed on bait, a chemical used to control fire ants, did not occur until 5 to 15 days after the animals were exposed. These effects would not have been detected with short-term (acute) bioassays.

TABLE 1

Relative Toxicity of Selected Pesticides to Shrimp, Fish and Oysters
Rank in Toxicity is Shown in Parentheses: (1) = Most Toxic
and (11) or (12) = Least Toxic (from Lowe, [illegible])

Pesticide	Shrimp 48-hour EC_{50}[1]	Fish 48-hour EC_{50}[2]	Oysters 96-hour EC_{50}[3]
	ppm (mg/liter)	ppm (mg/liter)	ppm (mg/liter)
Insecticides			
Dursban	0.0002 (1)	0.0012 (2)	0.27 (9)
Parathion	0.0001 (2)	0.015 (6)	22% decrease at 1.0 ppm (10)
DDT	0.0006 (3)	0.0036 (1)	0.014 (3)
Toxaphene	0.0042 (4)	0.028 (5)	0.028 (6)
DDT + Toxaphene + Parathion	--	--	0.05 (5)
Landrin	0.0042 (5)	1.7 (7)	No effect at 1.0 ppm (11)
Abate 4-E	0.020 (6)	No effect at 1.0 ppm (9)	0.17 (8)
Herbicides			
Igran	No effect at 1.0 ppm (9)	20% mortality at 1.0 ppm (8)	1.0 (9)
Weed-B-Gon (2,4-D + 2,4,5-T formulation)	No effect at 1.0 ppm (10)	Irritated at 100.0 ppm (10)	0.19 (7)
Fungicide			
Delan	0.15 (7)	0.010 (3)	0.0006 (2)
Miscellaneous compounds			
Corexit 7664 (oil-spill remover)	No effect at 1000.0 ppm (11)	No effect at 1000.0 ppm (11)	25% decrease at 32.0 ppm (12)
ET-346 (arsenical antifouling agent)	10% mortality at 10.0 ppm (8)	0.15 (6)	0.0021 (1)

[1] 48-hour EC_{50} = Concentration of pesticide in sea water causing 50% mortality or loss of equilibrium to juvenile penaeid shrimp.

[2] 48-hour EC_{50} = Concentration of pesticide in sea water causing 50% mortality to juvenile killifish (*Fundulus similis*).

[3] 96-hour EC_{50} = Concentration of pesticide in sea water causing 50% decrease in oyster shell growth.

The chemical analysis of residues is an important part of the bioassay program and other programs concerned with quantitative studies of pesticides. Our chemical assay project provides analyses for research projects at this station and for the National Monitoring Program. Details of our procedure for preparing and analyzing marine samples are available in a manual prepared by A. J. Wilson, Jr. (no date). A flow chart of the general procedure is shown in Fig. 2.

ECOLOGICAL STUDIES

A pollutant may be defined as any substance added to the environment which has a measurable and generally detrimental effect upon the environment. Thus, pollution such as the introduction of pesticides in estuaries is an ecological problem—interaction of the pesticide with biotic and abiotic factors of the environment. Therefore, we can no longer limit our studies of pesticides to any single factor in the environment. Investigations must also be made with populations of organisms which are interacting with their physical, chemical and biological environment.

Ecological studies at this station include observations on the effects of herbicides on the primary productivity of a coastal pond. Although much is known about the capacity of herbicides to eliminate undesirable plants, little is known on how they affect the biogeochemistry of the ecosystem. To determine this effect, Walsh and Heitmuller (1969) introduced a herbicide (Dichlobenil) into the water of a small (0.15 ha.) pond and used a similar but larger (0.91 ha.) pond for comparative purposes. *Chara vulgaris* and *Potamogeton pectinatus* were the dominant hydrophytes in both ponds. About 1 month after treatment, all of the *Potamogeton* and about 80% of the *Chara* were eliminated. The number of blue-green algae increased as the vascular hydrophytes died. Four months after treatment, the pond appeared as it did before treatment.

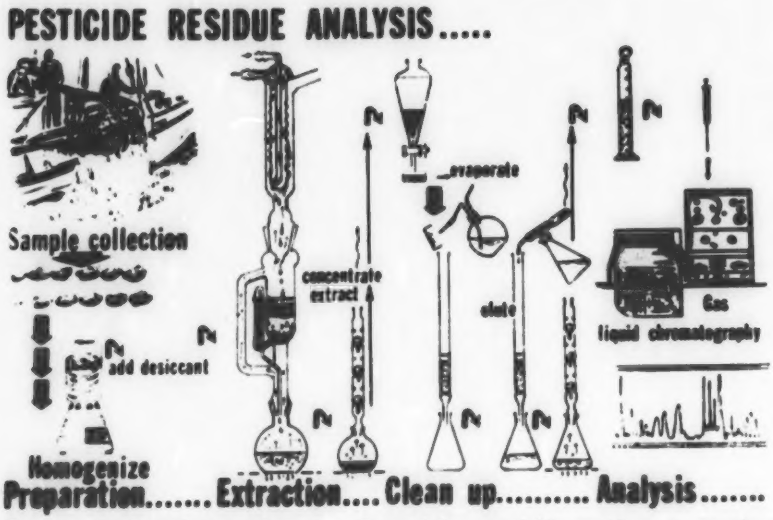
PESTICIDE RESIDUE ANALYSIS.....
Sample collection
add desiccant
Homogenize
concentrate extract
evaporate
elute
Gas liquid chromatography
Preparation....... Extraction.... Clean up.......... Analysis.......

FIG. 2. Analytical procedure for determining pesticide residues in marine organisms.

Other work with populations of organisms concerns the effect of pesticides on protozoans. These organisms, with algae and bacteria, form the broad basis of the aquatic food web. Also, as predators of bacteria, ciliates have an important role in regeneration of nutrients. Yet, few data are available on the sensitivity of ciliates to pesticides. N. R. Cooley (1969) found that the density of a population of *Tetrahymena pyriformis* grown in the presence of 10 ppm DDT was 26% less than that of an untreated "control" population. *Paramecium multi-micronucleatum* and *Paramecium bursaria* were sensitive to the chemical (Gregory, Reede and Priester, 1969). Work is in progress to determine how toxic effects of various insecticides are produced and which metabolic processes are affected.

The presence of pesticides in the water of an estuary could adversely affect the behavior of populations of resident fish or those that spend only a portion of their life cycle in these fertile nursery grounds. For example, if fish avoided water that contained pesticides, they might not be able to reach water of a particular salinity required for spawning or they could be forced out of the estuary to search for better quality water. Hansen (1969) investigated the capacity of sheepshead minnows, *Cyprinodon variegatus*, to avoid pesticides.

These fish avoided water containing DDT, endrin, Dursban® and 2,4-D. They did not avoid test concentrations of malathion or Sevin®. Fish exposed simultaneously to two different concentrations of the four pesticides avoided previously, avoided the highest concentration of 2,4-D but preferred the higher concentrations of DDT. Investigators are now determining the effect of DDT on the salinity preference of fish.

PHYSIOLOGICAL STUDIES

Sublethal concentrations of pesticides can cause subtle changes in the physiological processes of estuarine organisms. These changes are difficult to detect, yet they can be just as important as more evident effects from lethal doses. We are presently investigating the effects of pesticides on the blood of crustaceans and certain enzyme systems of fishes.

Nimmo and Blackman (1969) conducted physiological studies to determine the effect of DDT on the protein composition of shrimp blood and the distribution of this chemical in the shrimp. Preliminary investigations were made with grass shrimp *(Palaemonetes pugio)*, but white shrimp *(Penaeus setiferus)* and pink shrimp (*Penaeus duorarum*) were used in most studies. Pink shrimp exposed to 0.1 part per billion (ppb) of DDT showed a gradual decrease in the blood protein thought to be hemocyanin. Accumulation of DDT in shrimp was measured by analyzing whole-body residues. Residues were greatest in the hepatopancreas, least in the muscle.

Metabolic activity in fish, as in other animals, is dependent on enzyme activity and pesticides can interfere with this activity. Specifically, organophosphate pesticides inhibit cholinesterases, which are enzymes that function in the transmission of nerve impulses and ion transport. Holland, Coppage and Butler (1967) used the degree of inhibition of cholinesterase in brains of fish to measure organophosphorus pesticide pollution along the Atlantic and Gulf coasts. Coppage (1969) made laboratory tests to determine the relation of the toxicity of several organophosphate pesticides to *in vivo* inhibition of cholinesterase of sheepshead minnows. The enzyme activity of fish exposed to several pesticides was compared with normal enzyme activity in unexposed fish. Under test conditions, the number of fish killed by the organophosphates was proportional to the inhibition of cholinesterase in the brains of the fish, i.e., the greater the amount of inhibition, the larger the number of fish killed.

MONITORING PROGRAM

The Bureau of Commercial Fisheries has entered into cooperative agreements with state conservation agencies, and university and federal marine laboratories in 15 coastal states to establish a pesticide monitoring program. Shellfish were chosen as "indicator" organisms because they are sessile and readily concentrate pesticides from their environment, yet the chemical is flushed out of their tissues at a uniform rate when the pesticide is no longer present in the environment. Samples of oysters, clams or mussels, depending upon the estuary, are collected from about 170 stations at 30-day intervals and are analyzed for 10 or more pesticides. The samples are analyzed either by the collecting agency

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®Registered trademark: Dursban—Dow Chemical Co., and Sevin—Union Carbide Corp. Trade name does not imply endorsement of commercial products.

or at Gulf Breeze. More than 5,000 samples have been analyzed since July 1965.

The amounts of pesticides in shellfish vary according to the region in which the shellfish were collected and reflect the amounts of pesticides applied to crops within the particular drainage basin (Butler, 1966). For example, DDT residues in oysters from Willapa Bay, Washington, are low (20 ppb or less) and the drainage basin consists of forested slopes with little agriculture. Oysters from the south coast of Texas, however, contained 500 ppb. The basin in which these oysters were located drains an area that produces three crops a year and is treated heavily with pesticides.

PRESENT KNOWLEDGE AND FUTURE GOALS

Hayne, Duke and Sheets (1969) summarized the present state of knowledge about pesticides in estuaries as follows: "There is increasing apprehension based upon accumulating evidence of toxicity at low concentrations of chlorinated hydrocarbon and other pesticides and a growing body of facts about disturbance of the physiology at sublethal levels of these chemicals. An ambient level sufficient to promote body storage at measurable levels exists almost generally, at least for DDT. But there are very few known facts about the biologically effective levels in estuaries or about the populational effects of these levels. It is fair to say that we know and understand the problem only well enough to outline the areas where we need to know more."

Based on our knowledge to date, future research at this station will emphasize: (1) long-term tests on the effect of sublethal concentrations of pesticides on the physiology of estuarine organisms in sensitive stages of their life history, (2) investigations of the dynamics of pesticides in estuaries and (3) special studies of the movement and magnification of pesticides in estuarine food webs.

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PESTICIDE PROBLEMS IN WATER HYGIENE AND THEIR CORRECTION

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The Division of Water Hygiene recommends standards, limits and guidelines for a wide variety of chemical and biological contaminants of drinking water. Pesticides are among the chemicals for which limits have been recommended. The list of pesticides and the respective concentration limits of each are shown in Table I.

TABLE I

RECOMMENDED LIMITS FOR PESTICIDES IN DRINKING WATER

PESTICIDE	MAXIMUM PERMISSIBLE CONCENTRATION, mg/LITER[a]
Endrin	0.001
Aldrin	0.017
Dieldrin	0.017
Lindane	0.056
Toxaphene	0.005
Heptachlor	0.018
Heptachlor epoxide	0.018
DDT	0.042
Chlordane	0.003
Methoxychlor	0.035
Total organophosphorous and carbamate compounds[b]	0.1
2,4,5-TP 2,4,5-T 2,4-D[c]	Individual limits = 0.1 mg/liter; Sum of any combination of chlorinated phenoxy aklyl pesticides = 0.1 mg/liter

[a] For long term exposure.

[b] Expressed in terms of parathion equivalent cholinesterase inhibition.

[c] Short period limit only: 2 to 3 days, no more than once or twice a year.

In 1969, the Bureau of Water Hygiene conducted a Community Water Supply Study (CWSS) to determine if the American consumer's drinking water met the Drinking Water Standards. This study was designed to give an assessment of drinking water quality, water supply systems and surveillance programs in urban and suburban areas in each of the nine regions of the Department of Health, Education, and Welfare. These areas were selected to give examples of the several types of water supplies in the country.

A whole Standard Metropolitan Statistical Area (SMSA) was the basis of each study, except in Region I where the entire State of Vermont was included, with evaluations made on all public water supply systems in each study area. This coverage allowed an assessment of the drinking water quality of the large central city, the suburbs, and the smaller communities located in the counties in the SMSA, and the interaction between them.

Table II summarizes the pesticide data obtained from the analysis of 170 samples during the CWSS.

TABLE II

FREQUENCY OF OCCURRENCE OF INDIVIDUAL PESTICIDES IN CWSS

PESTICIDES	NO. OF TIMES DETECTED	% SAMPLES POSITIVE	MAXIMUM VALUE ppb	NO. OF SAMPLES ≥ 0.1 ppb
pp' DDT	79	46.4	<0.1	
Endrin	26	15.3	<0.1	0
Dieldrin	17	10.0	0.1	1 @ 0.1
Lindane	16	9.4	0.2	2 @ 0.2
Chlordane	13	7.6	0.2	1 @ 0.2
Heptachlor	11	6.5	0.2	2 @ 0.2
Heptachlor-epoxide	10	5.9	<0.1	0
Aldrin	7	4.1	<0.1	0

Only six samples or 3.5% of the total contained a residue at a concentration equal to or exceeding the reporting limit of 0.1 ppb. DDT was detected in almost 50% of the supplies. Aldrin was found in 7 supplies. It was determined that six of these were ground waters while one was a surface supply and it also contained four other residues. Toxaphene and methoxychlor were not detected.

A similar evaluation of water supplies was conducted in Tennessee in late summer of 1970. Twenty-six samples were analyzed for chlorinated pesticides; one contained 0.1 ppb chlordane, two contained <0.1 ppb pp'-DDT and the no residues were detected in the remaining 23.

Very little, if any, information is available concerning the quality of the water consumed by individuals and families not served by public or community water sources. A systematic survey of individual water supplies was conducted in four widely separated counties in Georgia. One of the objectives of the project was to examine a representative number of type of these supplies for pesticides as in the community water supply study. The 78 samples that were taken represented dug wells, bored wells, jetted wells, driven wells, springs and cisterns. Table III summarizes this data. Two interesting comparisons between this data and that of the community supplies is that DDT was detected in more than 60% of these supplies as compared to 46.4% of the community supplies. While only 3.5% of the community supplies contained a residue at a concentration ≥ 0.1 ppb the figure for the individual supplies is 9%.

TABLE III

FREQUENCY OF OCCURRENCE OF INDIVIDUAL PESTICIDES IN INDIVIDUAL WATER SUPPLY STUDY

PESTICIDES	NO. OF TIMES DETECTED	% SAMPLES POSITIVE	MAXIMUM VALUE ppb	NO. OF SAMPLES ≥ 0.1 ppb
pp' DDT	48	61.5	0.5	0.2, 0.3, 0.5
Dieldrin	5	6.4	<0.1	
Endrin	4	5.1	0.2	1 @ 0.2
Lindane	2	2.6	0.9	1 @ 0.9
Chlordane	2	2.6	<0.1	
Heptachlor	2	2.6	0.2	1 @ 0.2
Heptachlor-epoxide	1	1.3	0.2	1 @ 0.2
Aldrin	0	0	-	-

Table IV is a comparison of the distribution of pesticides in the community water supplies and the distribution in the individual supplies. It can be seen that about 10% fewer of the individual supplies were free of detectable residues. In the community water supplies, pp'-DDT was the residue that accounted for 80% of those samples containing one pesticide; the comparable value was 52% for the individual supplies.

TABLE IV

DISTRIBUTION OF RESIDUES IN THE WATER SUPPLY STUDIES

NUMBER RESIDUES DETECTED	COMMUNITY WATER SUPPLY STUDY		INDIVIDUAL WATER SUPPLY STUDY	
	Number	%	Number	%
0	72	42.4	25	32.0
1	56	32.9	46	59.0
2	18	10.6	4	5.1
3	13	7.6	2	2.5
4	8	4.7	1	1.3
5 & 6	3	1.8	0	0

The growing national attention to the use of 2,4,5-T has brought up the question as to whether this herbicide is getting into drinking water supplies where it may constitute a potential hazard to those who consume the water. There is very little information available at the present time to provide a basis for answering this question because monitoring of public water supplies in the United States for 2,4,5-T and related herbicides has been limited. It is generally recognized, however, that the contamination of drinking water supplies represents a potentially significant route for exposure of human beings to this material especially in those areas of the country where there is direct application of the herbicide to water for weed control and to a lesser extent where there is runoff from forested areas treated for brush control.

In the evaluation of public drinking water supplies the present maximum permissible concentration is 0.1 mg/liter (ppm) for either 2,4,5-T or the sum of any combination of 2,4,5-T and other related compounds as was shown in Table I. A survey was planned so that the results could be assessed in relation to this guideline in the future consideration of an ultimate standard for 2,4,5-T and other related herbicide in drinking water.

This survey was conducted during August through November 1970. Table V is a summary of the results of this survey.

TABLE V

OCCURRENCE OF PHENOXY ACID HERBICIDES IN 58 WATER SUPPLIES

HERBICIDE	WATER SUPPLIES IN WHICH HERBICIDE DETECTED		CONCENTRATION(ppb)		
	Number	Percent	Low	Medium	High
2,4,5-T	11	19.0	<0.5	<0.5	0.57
2,4-D	18	31.0	<0.5	<0.5	3.44
2,4,5-TP	4	6.9	<0.5	<0.5	<0.5

Analyses of the data obtained from this one-time sampling of community water supplies, which followed generally the period of seasonal use of 2,4,5-T and related herbicides, indicate that only traces of these herbicides could be detected in up to 19 to 31 percent of the water supplies. These trace amounts of 2,4,5-T and related herbicides, generally at concentrations less than 0.5 ppb and ranging up to 0.57 ppb for 2,4,5-T and 3.44 ppb for 2,4-D in the raw and/or finished waters, are extremely low when compared to the present Public Health Service guideline of a maximum permissible concentration of 0.1 mg/liter (ppm) for either the individual herbicide or the sum of any combination of these herbicides.

On the other hand, the survey substantiated the unquestionable fact that the use of 2,4,5-T and related herbicides on watershed areas and water supplysources results in the occurrence of the herbicides in the raw and/or finished waters of community water supplies. The lack of occurrence or the detection of 2,4,5-T and related herbicides at very low concentrations or in trace amounts in community water supplies in this survey could possibly be the source of a false sense of security from the public health standpoint.

The results of these surveys of drinking waters indicate that contamination of a water supply with a chlorinated pesticide in excess of values in Table I would be an exception rather than the rule. However, the water systems in many metropolitan areas are presently faced with several problems relative to the use of pesticides, insecticides, and herbicides. This includes their use by homeowners on lawns and around the foundation of their homes to control termites, by the farmers for agricultural control, and by utilities, highway departments, and local governments for controlling growth along right of ways.

LAWN AND TERMITE CONTROL

The use of pesticides and insecticides on lawns and for termite control is a concern of public health officials. All the substances tested during the CWSS have been and are being used for termite control. They are the so called hard pesticides, such as chlordane, dieldrin, endrin, aldrin, toxaphene, heptachlor, lindane, and DDT, which remain in the soil from six months to as much as seven years. In providing protection for a house, the exterminator jets a solution about eight feet into the ground all around the foundation and in the basement floor. The number of injections and amount of substance depends upon the size, shape, and other characteristics of the house. In the past chlordane was most widely used; however, dieldrin now seems to be more effective and to last longer. Registration of aldrin, dieldrin and mirex for all uses has been cancelled in recent weeks but they may still be in use.

The soft substances which breakdown faster require more frequent reapplications than the hard. At present the only soft substance being used is diazone. It is quite apparent that further study is necessary to determine which procedure should be used, hard agents with less frequent application or soft with more frequent applications, to insure that the potential hazard to public and private wells is eliminated.

SPECIAL INVESTIGATION OF A PRIVATE WELL

During the Community Water Supply Study, the Suffolk County, New York Department of Health staff investigated a private well supplying a house that had recently been treated for termites. A solution was used containing approximately 10,000 ppm of chlordane. It had been injected into the ground around the foundation and through the cellar floor. It was also sprayed on the wood just above the foundation. Based upon a noticeable change in the taste of the water, the county requested that the Bureau of Water Hygiene run the series of pesticide tests that were being done for the CWSS.

Of the ten pesticides tested, three were found in trace amounts similar to that found in public supplies: dieldrin, <0.1; heptachlor, 0.2; and heptachlor-epoxide, <0.1. However, 12.9 ppb of chlordane were found. This is over four times the limit of 3 ppb.

Although there was an old uncapped well nearby which might have been partially responsible, the fact that the well was only three feet from the house foundation would seem to indicate a problem regardless of the old well.

Many of the older houses in that county have their wells close to house foundation or in the basement. Presently the county sanitary codes require only a three foot space between the house foundation and its well. In view of these facts, it is hard to imagine such wells as not becoming contaminated.

The owner of the contaminated private well, at the request of the county staff, pumped his well fairly constantly over a five to six week period. A second sample was taken and also forwarded to the Gulf Coast Water Hygiene Laboratory for analysis. The tests on this sample showed 1.5 ppb of chlordane with none of the other substances being detected.

The foregoing discussions, although based on a private well case, clearly indicate needs in several areas. A complete investigation should be made as to the entrance of pesticides into ground water, their persistance, and their rate and distance of travel. Such information is needed to insure the future protection of public water supply ground water sources.

AGRICULTURAL CHEMICALS

In the past, all the substances tested for during the water supply studies were used on crops. However, over the past five years they have gradually been replaced with new ones. These are too numerous to enumerate here; however, as an example, the 1970 Potato Crop Control Recommendations for the State of New York are listed below.

Seed Treatment
  Captan
  Polyram
  Dithane

Weed Control
  Per Merge
  linuron
  Patoran
  Eptam
  amitrole

Insect Control
  parathion
  endosulfan (Thiodan)
  carbaryl (Sevin)

Blight Control
  maneb
  Dithane
  Manzate
  polyram
  Daconil
  Difolatan
  nabam
  duter

Additional chemical suggested for other purposes include:

Vapam
maleic hydrazide
Chloro-IPC
Fusarex

Expanding the foregoing list to a nationwide basis, the necessity for constant research relative to the possibility of such chemicals getting into water supplies, surface and ground, is obvious. Such questions as does the chemical persist in being carried through the soil to the wells or over the ground to the reservoir, how far away from drinking water source should the chemical be applied, and most important is the chemical a health hazard when consumed by man through water must be answered. Another important consideration that metropolitan health officials must consider is the use of irrigation wells as water supply sources as farms disappear and suburbia takes over.

WEED AND BRUSH CONTROL

Many herbicides in addition to 2,4,5-T, 2,4-D and 2,4,5-TP are used for weed control along highways, railroads, power transmission lines, etc. Following is a list of such compounds that have been used in watersheds as they serve as water supplies. Aquathol Plus (disodium 3,6-endoxohexahydrophthalate), Radapon and Dalpon (2,2-dichloro propionic acid), Tordon (4-amino-3,4,5-trichloro picolinic acid), Simazine 80W (2-chloro-4,6-bis-(ethylamino)-s-triazine), Bromacil (50-bromo-3-*sec*-butyl-6-methyluracil).

The only drinking water standard that exists to protect the consumer from harmful organic chemicals other than phenols, detergents and those pesticides listed in Table I is the carbon-chlorform extract. Two hundred micrograms of these substances per liter of drinking water are allowed. It has been estimated that activated carbon removes only 10% of the organic matter from water. Therefore, probably the greatest problem facing chemists in the field of water hygiene today is the identification of organic compounds, including pesticides, found in drinking water so that proper standards can be set.

SUMMARY OF THE

NATIONAL PESTICIDE MONITORING PROGRAM

Sponsored by the
Working Group on Pesticides
Washington, D.C.
October 1970

Purpose

The purpose of this summary is to provide information on the National Pesticide Monitoring Program. While this program is not new, neither has it been widely publicized. Greater emphasis on environmental problems and increased participation on the problem-solving process nationwide suggests a commensurate need for an awareness of ongoing efforts.

The objective of the National Pesticide Monitoring Program is to establish baseline levels of pesticide incidence in substrates of food and feed, humans, soil, water, air, wildlife, fish and estuaries and to assess changes in these levels. Baselines are needed as a norm against which to compare subsequent data to determine what is an increase or decrease in pesticide levels. Sampling for a variety of pesticides is to be statistically sound and on as randomized a pattern as can be attained.

Monitoring of each substrate of the program is conducted by a federal agency and its cooperators having a corresponding mission. The design and scope of sampling are reviewed by the Working Group to assure national monitoring coverage in terms of "problem-finding." Agencies conduct this monitoring in addition to their own mission-oriented monitoring, which is for the specific purpose of "problem-solving." The willingness of agencies to participate in this important program, particularly under increasing budgetary constraints, is an exemplary instance of interagency cooperation.

Data developed within the National Pesticide Monitoring Program are generally submitted for publication in the Pesticides Monitoring Journal, which is also sponsored by the Working Group on Pesticides. An issue of the Journal, early in 1971, will contain the revision of a recommended list of pesticides for which to monitor. Important among additions to the list are polychlorinated biphenyls (PCB's).

Additional inquiries on the National Pesticide Monitoring Program may be referred to:

Dr. William S. Murray
Executive Secretary
Working Group on Pesticides (CS-22)
Parklawn Building, Room 11-82
5600 Fishers Lane
Rockville, Maryland 20852

Food and Feed Monitoring

The federal program for monitoring pesticide residues in food and feed is comprised of surveillance programs maintained by the Food and Drug Administration and also in the U. S. Department of Agriculture. The objective of this monitoring program is to determine the levels of pesticide residues in unprocessed and commercially processed consumer food commodities, animal feeds and composites of food items prepared for human consumption.

Specific programs being carried out to accomplish this objective include the following:

a. A continuing Market Basket Study to determine pesticide residues in food ready to be eaten;

b. Nationwide surveillance of unprocessed food and feed;

c. Analysis of meat and poultry samples taken from animals at time of slaughter.

The Market Basket Study consists of collecting the entire 2-week diet of a 16- to 19-year old male. Thirty such baskets are collected annually - six baskets in each of five geographical areas. The 120+ items in the diet are divided into 12 groups, e.g., dairy products; fruits; vine and ear vegetables; meats, fish and poultry; etc., for examination.

The food and feed surveillance program is carried on by 17 field districts. The program requires sampling of individual items of food or crops at their origin. Approximately 6,000 samples are examined under this program.

The meat and poultry surveillance work involves the analysis of approximately 3,500 samples of meat and 3,000 samples of poultry taken from 1,200 of the major processing centers.

Human Monitoring

The purpose of this program is to determine on a national scale the current levels and trends in levels of certain pesticide chemicals in the general human population and to aid in the determination of their potential significance to man.

Since tissues must continue to be collected through pathologists and medical examiners, the sampling population is drawn from sources in cities of 25,000 or more as of the 1960 census. (It is recognized that rural citizens are referred to nearby hospitals when such care is needed.) The country was divided into four census regions. Under this plan, 1,590 samples of adipose tissue are collected and analyzed each year.

A 12-month quota for each collecting site was established based on a breakdown by sex, age and race, reflecting census data over the country. There are three age groups: 14 years and under, 15 through 45 years and 50 years and over; these are allocated proportionately.

Tissues are collected from surgical and post-mortem specimens, without regard to the patient's stated occupation. Excluded are: (1) known or suspected acute pesticide poisonings; (2) chronic debilitating illnesses, i.e., terminal carcinoma, tuberculosis, long-term comotose patients, etc.; and (3) institutionalized patients.

This random scheme for human monitoring is not intended to fulfill the entire epidemiological requirements for determining the effect on human health of continued long-term exposure to pesticide chemicals. This program responsibilitity is being met by the 15 Community Study contract projects which are pursuing prospective studies of control and occupational exposure populations in each study area. These contracts are generally located in areas of heavy pesticide usage. At each of these sites, some tissues (especially blood) are sampled to complete the epidemiological picture. States with Community Studies projects are: Arizona, California, Colorado, Florida, Hawaii, Idaho, Iowa, Louisiana, Michigan, Mississippi, New Jersey, South Carolina, Texas, Utah and Washington.

Also, 14 state technical assistance or demonstration pesticide projects in state health departments of other states collect tissue samples for human monitoring in their state. This collection is in addition to the basic statistical design and may be more problem oriented, selection being based at least in part on pesticide usage and morbidity-mortality determinations in the state. States where these projects are located are: Alabama, Arkansas, Illinois, Kentucky, Kansas, Maine, Montana, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, South Dakota and Tennessee.

Soil Monitoring

Soil is one of the most significant storehouses of pesticide residues in the biosphere. Soil serves as a reservoir from which pesticides can enter food and feed crops, can be carried into the atmosphere attached to particulates, and can be carried into the hydrosphere by runoff to serve as an auxiliary storehouse. Soil serves as the source of pesticides for uncounted soil organisms, which, in turn, serve as food for other organisms. For these reasons alone, the knowledge of pesticide burden in the nation's soils becomes important - knowledge best gained from a well-designed monitoring program.

The soil monitoring program is statistically designed to give reasonably reliable estimates of pesticide levels in U.S. soils with reference to land use. Two major land uses are included - cropland and noncropland. Ten-acre sites were randomly selected at the rate of one site per 40,000 acres of cropland and one site per 400,000 acres of noncropland. That rate of sampling yielded 9,468 cropland sites and 3,822 noncropland sites. The sampling schedule cycles in 4 years; one-fourth of the sites (3,325) are sampled each year. The program was initiated in FY 68 when six states were sampled. In FY 69, cropland was sampled in 43 states and noncropland in 10 states. In FY 70, cropland was sampled in 35 states.

When repeated efforts failed to obtain funds necessary to support the program, the agency was forced to redirect the monitoring efforts planned for FY 71. As a result, only a small portion (Corn and Cotton Belts) of the program is retained. A plan for monitoring urban soil is as yet unimplemented.

Water Monitoring

A monitoring program for the presence of pesticides in the hydrologic environment provides for a continuing assessment of the general levels of pesticides in the nation's water courses and bottom sediments. Quarterly water samples and semi-annual bed material samples are collected at 161 sites in the continental United States, Alaska, Hawaii and Puerto Rico. Sampling sites were chosen at random from hydrologic units within the 20 major drainage basins defined by the Water Resources Council.

The network of stations selected is designed to assess general levels of pesticides in runoff; thus, lakes, which may contain an improportional amount of runoff for their area, are not monitored under this part of the program. Bottom sediments are monitored because it is known that many of the pesticides entering streams with runoff are contained in or sorbed on suspended soil particles.

A request has been made for funding as part of the National Water Data Network implementation in FY 72.

Air Monitoring

The air monitoring component of the program has not yet been implemented pending resolution of instrumentation and priorities by the responsible agency. Air monitoring should be conducted randomly without special consideration for a particular or limited part of the environment (such as human habitats or industrial centers). Air sampling should be conducted in a minimum of 40 to 60 separate areas of the country; the boundaries of these areas should be determined by longitude and latitude or by some other grid.

When an instrument system has been designated, its limitations will dictate sampling interval and time required for analysis of each sample.

The suggested 40 to 60 locations will be adequate to assure that resultant data can be correlated with that developed in other parts of the National Monitoring Program. Funding will determine the number of samples collected.

Wildlife Monitoring

The wildlife monitoring program includes the measurement of levels and trends of pesticides in three kinds of birds - black and mallard ducks, eagles, and starlings.

Duck Wing Monitoring: Duck wings from all parts of the nation are made available for monitoring as a byproduct of an annual nationwide survey of waterfowl in which hunters mail thousands of wings to central collection points for biological examination. Wings of mallards and black ducks are used because the combined range of these two species covers the continental United States.

Mallard wings from most states and black duck wings from Eastern States are first segregated into state groups of immature and adult wings, and each group is then systematically sorted into pools of 25 wings each. A random sample of these pools, roughly proportional in number to a state's mallard or black duck harvest, is selected for pesticidal analysis.

Two years of sampling data are now available - 1965 and 1966. Since small differences were detected in residue levels between the 2 years, there may be justification for scheduling wing monitoring hereafter at 2- to 3-year intervals. Sample sizes appear adequate and the data have received satisfactory statistical treatment.

Eagle Monitoring: Eagles have been monitored for a number of years by the Bureau of Sport Fisheries and Wildlife as part of this agency's in-house research program. They are included in the national pesticide monitoring program even though no well-established pattern of sampling is possible. Only birds which are found dead or are incapacitated and beyond recovery are made available for analysis. Twenty-one golden and 45 bald eagles were collected in 1964 and 1965 in 18 of the continental United States and two Canadian provinces. Analyses of carcasses, livers and brains were performed by the Patuxent Wildlife Research Center. Plans are to continue monitoring the bald eagle as part of the nationwide program.

Starling Monitoring: The starling monitoring protocol calls for collections to be made at two periods of the year - late summer and early winter. Three composite samples of 10 birds each are to be collected per seasonal sampling period at each of 44 collection sites widely distributed geographically. Samples may be taken by trapping or shooting.

To date, starlings have been sampled at 128 sites in August-September 1967, in January-February 1968 and in November 1968. Sampling sites were selected randomly among the 48 continental states.

Fish Monitoring

Beginning in fall of 1970, 50 new stations were added to the existing 50 stations sampled annually for monitoring residues in fish. The original 50 stations, sampled since the spring of 1967, will be retained in the expanded program. Criteria for selection of specific station locations included the following, in order of priority: (1) availability of desired species of fish; (2) location near the mouth of major rivers to determine pesticide contribution from the drainage area; (3) relationship to station locations for other phases of the National Pesticide Monitoring Program, particularly those stations used for monitoring surface waters; (4) existence of state-sponsored monitoring program or cooperative participation by state conservation agency; and (5) availability of suitable manpower and facilities to make field collections.

Three composite samples, each containing three to five adult fish of a single species, are collected. All composite samples are replicated for a total of 600 samples. Residue analyses are performed for the identification and quantification of a number of pesticides, including mercury. Samples are screened for the presence of interfering polychlorinated biphenyl compounds.

Estuarine Monitoring

The estuary is an important environment since pesticides are carried to it through river basins. Oysters and clams found in estuaries are well suited for pesticide monitoring because of concentration and retention of residues for extended periods following exposure.

Pesticide levels in oysters and clams are monitored monthly at 170 coastal locations in the U.S. Samples are normally collected under contract with states. Actual sampling points within an estuary are selected on the basis of hydrographic data and the availability of suitable shellfish populations.

As future funding of this component of the program permits, attention is expected to be given to the addition of several coastal states in the sampling work, problems of randomicity, inclusion of mollusk bed sediments, and the expansion of the types of pesticides monitored for.

PESTICIDES IN SOILS AND CROPS

B. J. Stojanovic and Fay Hutto

INTRODUCTION

Pests are considered our most serious competitors for the essentials of our existence and survival. Our crops and livestock compete in a complex and hostile environment shared by about 50,000 species of fungi that cause more than 1,500 diseases, 30,000 species of weeds (more than 1,800 of these cause serious economic losses each year), 15,000 species of nematodes, and more than 10,000 species of pest insects.[1] Our defense against pests includes many different agricultural practices, one of which is the use of effective chemical methods of control or the use of pesticides.

The need for pesticides in our total scheme of things has long been established, although often criticized. It is generally recognized that without pesticides many of the foods that we now take for granted would be luxury items available only to a few. Proof of what can be done in protecting crops from pests and in increasing production has been amply demonstrated. There is no doubt that pesticides have helped to improve the quantity and quality of the crops raised in this country over the years. The use of pesticides has enabled fewer farmers to produce more crops to feed ever increasing urban populations. The foods we buy today are freer from pest damage than ever before; fibers and grains are more plentiful; and the forest and the feed lots are more efficient and more useful to us than they have ever been before.

Some 550 basic chemicals are commonly used in agriculture, and these are commercially presented in about 50,000 different formulations under many trade names. They are used to control insects (insecticides), weeds (herbicides), ticks and mites (acaricides and miticides), plant parasitic fungi (fungicides), and rodents and carnivores (rodenticides). Based on their physical states, pesticides are used as solids (dusts, baits, granules, etc.), liquids (solutions, suspensions, emulsions), and gases (fumigants, vapors).

Soil receives pesticides either directly by the application of chemicals to the soil, as in weed control, or indirectly by the use of pesticides for control of insects on agricultural crops. Insecticides are normally directed to the leaf surfaces of a plant, but a substantial portion usually misses the plant and is deposited on the surface of the ground. More is added by the runoff from the plant and with the dead remains of the plant which invariably contain small amounts of pesticides. Rainfall and normal cultivation carry some of the applied pesticide materials into the soil itself. In addition, many waste pesticides and empty pesticide containers are disposed of (buried) in the soil. Regardless of the channel through which pesticides find their way into the soil, their presence may upset the ecological balance of the soil population or modify soil chemical characteristics. In addition they may persist and, through excessive accumulation, render soil infertile or crops unconsumable. The ultimate fate of pesticides in soil depends upon biological, chemical, or physical processes operating singly or in sequence.

It is not the purpose of this presentation to try to digest all the technical background of this complex subject, nor is it the intention to parrot back what has been read on the fate of pesticides in soils and crops. An attempt will be made to present some highlights of the fate of pesticides in soils and crops and to focus a part of this discourse on certain problems closely associated with pesticides being deposited on the land.

WHAT IS SOIL?

Without turning this presentation into a basic course in soil, we would like to discuss briefly a few pertinent soil-related concepts.

Like many commonplace features of nature, soil is something that can be found most everywhere and has apparently always been with us. To many of us, agricultural soil is dirt. This unjust reference is the result of a lack of understanding of what soil is, where it comes from, and what its basic properties are. However, the housewife would be justified in referring to soil as dirt when, because of its specific characteristics (stickiness), it has a tendency to cling to shoe soles and eventually to carpets. Soil out of place is dirt, just as corn, cotton, or soybean plants are weeds when out of place.

There are different concepts and viewpoints regarding this important product of nature. For example, to a mining engineer soil is the debris covering the rocks of minerals which he must quarry. To the highway engineer soil is the material on which a road is to be built. The farmer and the homeowner look upon soil as a habitat for plants. The farmer makes a living from the soil, and to him it is more than useful - it is indispensable. A textbook edaphological* definition of soil is stated as follows: "The soil is a natural body, synthesized in profile form from a variable mixture of broken and weathered minerals and decaying organic matter, which covers the earth in a thin layer and which supplies, when containing the proper amounts of air and water, mechanical support and, in part, sustenance for plants."[2]

Soils consist of mineral and organic matter, water, and air combined in three phases: solid, liquid, and gaseous. There are many kinds of soils or soil types, and throughout the world there must be hundreds of thousands of soils. Differences between neighboring soils generally reflect changes of such factors as topography, drainage, or parent material. Regional soil differences are generally greater than those of local associations of soil types and often reflect variation in climate and distribution of living organisms. For example, soils of the arid Western States are neutral or alkaline in reaction and very low in organic matter. Clay minerals of the montmorillonite expanding-lattice types predominate in these soils. The soils of the humid Southeast, on the other hand, are acid and contain appreciable quantities of organic matter. Kaolin and the hydrous oxides of iron and aluminum predominate in the clay fraction.[3]

THE FATE OF PESTICIDES IN THE SOIL

The fate of a pesticide in the soil is dependent chiefly upon interaction between the chemical and its environment. Therefore, pesticidal behavior cannot be predicted from studies with a single soil or from a single pesticide on several soils.

This report considers seven factors which are known to affect the fate and behavior of pesticides in soils. These factors are as follows: (1) adsorption and desorption, (2) chemical decomposition, (3) photochemical decomposition, (4) microbial decomposition, (5) volatilization, (6) movement, and (7) plant and microbial uptake.

ADSORPTION AND DESORPTION OF ORGANIC PESTICIDES IN SOILS

Adsorption is considered to be one of the chief factors influencing the interactions taking place between pesticides and the inorganic and organic fractions of the soil. The process of adsorption affects directly or indirectly the magnitude of the effect of the other six factors, particularly that of biodegradation and bioactivity of pesticides in soils. The adsorption-desorption phenomenon between pesticides and soil colloids is due to the attraction or repulsion between a solid surface and a vapor or solution.

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* Edaphology is the study of the soil from the viewpoint of higher plants. It considers the various properties of soils as they relate to plant production.[2]

Adsorption is attributed to one or more of the following mechanisms: (1) physical adsorption, (2) hydrogen bonding, (3) coordination complexes, and (4) chemical adsorption.[4] Physical adsorption is due to van der Waals forces, i.e., the weak, non-specific purely molecular forces.[5] Adsorption resulting from hydrogen bonding consists of a bond between two highly electronegative atoms through the medium of the hydrogen atom.[6] Recent evidence suggests that the coordination type of bonding is quite important in determining the fate and behavior of pesticides in soils. Coordination compounds or complexes are those that contain a central atom or ion, usually a metal, surrounded by a cluster of ions or molecules.[7] Chemical adsorption involves coulombic forces and is an outgrowth of bonding between the adsorbent (soil fraction) and adsorbate (organic pesticide).[4] A coulomb is defined as the quantity of electric charge transported by a current of one ampere in one second.[5] The forces involved in chemical adsorption are stronger than those involved in any of the other three adsorption mechanisms.

Regardless of the actual mechanism of adsorption, there are two groups of factors that affect adsorption and desorption of pesticides by soil colloids: microfactors and macrofactors.[4] The microfactors include the nature of the soil colloid, the nature of the adsorbate (pesticide), soil reaction (pH), the saturating cation, soil moisture content, temperature, and the nature of the pesticide formulation. The two macrofactors are the physical properties of soil as a substrate and the influence of climate.

One of the fundamental factors affecting the extent of adsorption is the nature of the soil colloid. Colloids, such as organic matter or montmorillonite and vermiculite clays, which have high cation exchange capacities and surface areas, have great capacities for adsorption by both the physical and chemical mechanisms.[4] On the other hand, the clay minerals such as illite, kaolinite, and chlorite, because of their low cation exchange capacities and surface areas, do not have very large adsorption capacities. A study on adsorption of s-triazine herbicides on humic acid showed that adsorption of atratone, atrazine, prometone, and prometryne increases when the amount of calcium humate at a specified calcium saturation is increased.[8] However, increasing the calcium saturation of humic acid from 10 to 100% results in decreased adsorption. Moreover, montmorillonite has been reported to adsorb considerably more of various herbicides than illite or kaolinite,[9] and adsorption of monuron is highest in soils in which montmorillonite is the major clay constituent.[10]

The nature of the pesticide, as well as that of the soil colloid, influences adsorption. Even within the same family, some pesticides are more strongly adsorbed than others on a given soil colloid.[4] Within a family of herbicides there appears to be some relationship between solubility and adsorption.

For example, increased chloro-substitution on the aromatic ring of phenoxyacetic acids reduces solubility of these acids. Moreover, there is a strong inverse correlation between solubility of these compounds and the extent of their adsorption.[11] However, the inverse relationship between adsorption and solubility appears to be valid only within a family of compounds.[12] A study on adsorption of representative members of various herbicide famiies showed that there is no general relationship between water solubility and degree of adsorption when comparing molecules of widely different natures. In this case the chemical nature of the particular compound is the important factor affecting the extent and type of adsorption. Organic acids and ketones have been reported to be adsorbed on clay surfaces by formation of a hydrogen bond between the carbonyl group and the clay particles.[13,14,15] On the other hand, adsorption of certain substituted ureas and s-triazines in an acid environment is due to ion exchange.[9] Moreover, dithiocarbamate fungicides, which are highly ionized in solution, may be retained by the soil-clays through coulombic forces.[6]

Adsorption studies with well-characterized mineral adsorbents have clearly shown that the extent of adsorption of many pesticides is pH dependent. In general the adsorption of various herbicides with widely different molecular structures increases as the pH decreases with the pH at which maximum or minimum adsorption occurs being a function of the particular compound and the adsorbent.[9] This trend of pH dependence also occurs on certain organic adsorbents. For example, the adsorption of 2,4-D by a hydrogen cation exchanger is nearly twice as great at pH 2.5 or below than at pH 3.3.[16] This dependence of the extent of adsorption on pH is due to the fact that pH determines the degree of association or dissociation of pesticide molecules and, therefore, the amount which is adsorbed.

The saturating cation in a soil may also affect the degree of adsorption. There is a definite difference among inorganic cations in their ability to exchange for another cation present on the exchange site, and there may also be a difference in the replacement of an organic cation (adsorption of an organic molecule) as a function of the nature of the inorganic cation present on the exchange complex. Adsorption of ethylene dibromide vapors by oven dry clay minerals is on the order of Na > Ca > Mg.[17]

The moisture content of the soil system appears to have a great effect on the degree of pesticide adsorption. In many cases herbicides, which are susceptible to volatilization are more effective in dry soil than in moist soil.[18] Under low moisture conditions the compound is adsorbed but the binding energy is sufficiently low that the pesticide material is biologically available to produce the desired effect. However, in the case of a soil with a high moisture content little of the pesticide is adsorbed. Most of it remains in the soil solution where it is susceptible to vapor loss, and upon vaporization there remains an insufficient amount of material to produce the desired metabolic effect. An excellent illustration of this phenomenon is the vapor loss of DNBP which is greater from wet soil than from dry soil.[4]

High moisture content, however, does not always decrease the effectiveness of pesticides.[4] Diuron is more toxic to cotton under moist conditions than under dry conditions. This pesticide has a fairly low vapor pressure and is strongly adsorbed under dry conditions. However, under moist conditions desorption may occur, and with no appreciable volatilization loss the concentration of diuron in the soil solution increases sufficiently to kill the plant.[4]

Adsorption processes are exothermic, while desorption processes are endothermic in nature. Therefore, an increase in temperature would be expected to reduce adsorption and favor desorption. Studies on the effect of temperature on the adsorption of various herbicides by different adsorbents indicate that this temperature-adsorption relationship does not hold in all cases.[12] While adsorption of simazine, atrazine, and monuron by bentonite is greater at 0°C that at 50°C, diquat is completely adsorbed at both temperatures. In the case of a muck soil the extent of adsorption of all these compounds is similar at both temperatures. In addition, the extent of desorption or adsorption of the herbicides as a function of increasing or decreasing temperature appears to be reversible.[12]

Temperature may also exert an indirect influence on adsorption through its effect on solubility.[4] In general, solubility and temperature work together with both leading to decreased adsorption as the temperature rises. Moreover, the vapor pressure of organic compounds is temperature dependent with an increase in temperature causing an increase in the vapor pressure of the compound. Since both adsorption and vapor pressure are temperature dependent, one would expect that with a compound with high vapor pressure at low temperatures, an increase in temperature would favor desorption and concomitantly increase the vapor pressure and vapor loss of the compound. This is the case with DNBP, EPTC, and CDEC.[12]

To overcome many of the mechanical problems of pesticide application, various types of formulations are used. Many of the herbicides can be formulated in the acid, salt, or ester form. Although the metabolic efficacy of these three forms may be nearly the same in a nutrient solution, their behavior and bioactivity in the soil may vary widely because of differences in the physical properties between the three forms. The chemical natures of other materials used in formulations (solvents, emulsifying agents, surftactants, etc.) may also drastically affect interaction between the pesticide and the constituents of the soil system. For example, comparison of the availability of the butyl ester and triethanolamine forms of 2,4-D in a mixture of sand and montmorillonite indicates that the ester form is fixed more strongly than the salt form.[4]

The microfactors which have been discussed exert a direct influence on adsorption and desorption of pesticides by soil colloids. On the other hand, the macrofactors indirectly influence these phenomena by affecting the periodicity and amount of moisture at the soil surface as well as entrance of moisture into and through the soil profile.[4]

Two of the physical properties of soil, pore size and pore size distribution, are determined to a great extent by the structure of the soil.[4] In a gross sense, these parameters affect the rate at which water enters and moves through the soil. The greater this rate, the greater the volume of water that will move past a given reference point per unit of time. This movement should have some effect on the equilibrium between the pesticide in the soil solution and that adsorbed on the soil colloid. From the standpoint of both mass action and solubility, it would appear that desorption would be increased. The extent of desorption under these conditions would also be related to the nature of the adsorbate and adsorbent and to the binding energy of the adsorbate-adsorbent complex.[4]

Climatic factors may also indirectly affect adsorption and desorption of pesticides.[4] For example, if the climate causes the surface inch or so of the soil where the pesticide is located to become and remain extremely dry for long periods of time, the pesticides may be highly adsorbed. However, in areas with frequent rainfall the moisture level of the soil may remain at such a high level that the pesticide would be desorbed.

CHEMICAL DECOMPOSITION OF ORGANIC PESTICIDES IN THE SOIL

There is nothing magical about the fundamental chemistry of pesticides. Reactivity characterizes pesticides, and in the test tube they undergo many of the same reactions as do other organic molecules. As in the laboratory, the chemical degradation of pesticides in soil involves the attack of a reagent on a reactive compound. Because of its structure soil presents an effective medium for the conduct of such reactions because it permits the confluence of oxygen, water surfaces, and pesticides with the soil constituents.[19] Many different types of chemical reactions involving decomposition of pesticides occur in soil, but most of these reactions can be classified as either catalytic or hydrolytic reactions.

A catalytic reaction is one whose rate is greatly increased by the presence of a chemical substance which remains unchanged after completion of the reaction.[20] Although the catalyst appears not to be involved in the reaction, it actually takes part in the reaction and is regenerated in its original form when the reaction is completed. In the soil many pesticides undergo catalytic reaction with the catalyst being some substance present in either the organic or mineral fractions of soil. For instance, the presence of basic amino acids in soil organic matter catalyzes hydrolysis of organophosphorus esters[21] and the dechlorination of DDT and lindane.[22] Other nitrogenous soil constituents, the reduced porphyrins, have been shown to reductively dechlorinate halogenated hydrocarbons such as DDT.[23] The mineral fraction of soil is primarily siliceous and so, in bulk, is inert toward chemical reactions with pesticides.[19] However, the presence of less abundant minerals such as carbonates and sulfides provide more reactive possibilities. Those containing iron, manganese, cobalt, and other transition metals take part in or catalyze oxidations and reductions. For example, the dechlorination of DDT and other chlorinated hydrocarbons in alkaline solution is catalyzed by iron salts.[24,25,26] The oxidation of organic sulfides (thioethers), sulfites, and phosphites to the corresponding sulfoxides, sulfates, and phosphates can also be catalyzed by minerals.[19] Moreover, acidic or basic sites on clay minerals can catalyze pesticide reactions. In the dry form, for example, clay catalytically decomposes endrin and heptachlor.[27,28]

A second important reaction of many pesticides is their hydrolysis or reaction with water. This reaction is highly dependent on pH. While a few pesticides such as captan[29] are hydrolyzed at neutrality (pH 7), most hydrolysis reactions proceed more rapidly at either high or low pH than in the neutral range. Since soil water is seldom neutral and its pH may vary from strongly acid (pH 3) to strongly basic (pH 10.5), it is an excellent reaction medium for these reactions. Many types of pesticides such as carbamates[30], organophosphates[31], and phenoxyacetic acid esters[19] undergo alkaline hydrolysis.

In many cases hydrolytic reactions are interrelated with catalytic reactions. In other words, hydrolyses which would proceed slowly in aqueous solution are speeded up by the presence of various minerals in the soil. For example, cupric ions[32,33] and copper-montmorillonite suspensions[34] have been shown to catalyze hydrolysis of some organophosphates.

This cursory discussion of chemical degradation of pesticides contains only a brief discussion of the chemical reactions that pesticides may undergo. However, it emphasizes the fact that pesticides, because of their property of chemical reactivity, do undergo nonbiological degradation in soil.

PHOTOCHEMICAL DECOMPOSITION OF PESTICIDES

Photochemical decomposition is the breakdown of matter under the influence of light. While pesticide photodecomposition undoubtedly has little importance in the non-biological degradation of pesticides within the soil itself due to lack of light penetration, photochemical transformations do take place on the surface of the soil.

Most pesticides undergo light-energized transformations in aqueous solution or suspension.[35] Although the effective energy range of sunlight is narrow (from about 290 mu to about 450 mu), this span is sufficient to provide for the rupture of many types of chemical bonds. Laboratory investigation has revealed that light within the wavelength range of sunlight energizes quite a variety of common reactions including oxidation, reduction, elimination, hydrolysis, substitution, and isomerization.[36] Usually air, water, and light combine to produce a multiplicity of reactions. For example, phenoxy herbicides undergo oxidation, reduction, substitution, and probably, hydrolysis in aqueous solution when activated by sunlight in air. The final oxidation, which is not photochemical, produces a dark polymer whose physical and chemical properties are identical with those of natural and artificial humic acids.[37]

Photo-oxidations are among the most general and important environmental reactions. The variety of ways in which oxidation can occur is demonstrated by aqueous solutions of the herbicide monuron [3-(p-chlorophenyl)-1, 1-dimethylurea]. By one route the N-methyl groups are removed successively to form p-chlorophenylurea, while by another method the aromatic ring of monuron is hydroxylated.[38]

Photoreductions also occur as illustrated by the rapid formation of 1-methylnaphthalene from 1-naphthaleneacetic acid in water.[39] This instance also provides a good example of the importance of photooxidation because the final products from photolysis of methylnaphthalene and 1-naphthaleneacetic acid are the stable, oxidized forms of phthalic and naphthoic acids, respectively.

Elimination reactions are also represented among the environmental transformations energized by light. For example, N-methylcarbamate insecticides such as carbaryl are known to undergo alkaline hydrolysis to produce 1-naphthol, methylamine, and carbon dioxide. However, photolysis under neutral conditions or in nonaqueous solvents leads to 1-naphthol and methyl isocyanate by elimination.[40]

Even some of the most persistent organic pesticides may be photolyzed. For example, methoxychlor in aqueous alcohol can be photochemically degraded.[41] Moreover, ultraviolet light catalyzes degradation of DDT in aerobic and anaerobic environments.[42]

While the body of information on photochemical reactions of pesticides is far from complete, the existing information indicates that these reactions on the soil surface probably constitute a major pathway of nonbiological pesticidal degradation.

MICROBIAL DECOMPOSITION OF ORGANIC PESTICIDES IN SOILS

When the activity of a pesticide is diminished or impaired by its adsorption to soil inorganic and organic colloids, the potential for pollution nonetheless remains, should the adsorbed toxic molecule revert back to a biologically active form. Of the several mechanisms by which pesticides may be detoxified in soil, microbial degradation appears to be by far the most important. Biodegradation in general is considered to be a process of conversion by microorganisms of pesticides into one or more simpler, non-toxic substances. When oxygen is available, the final products of degradation will be carbon dioxide, water, sulfate, nitrate, phosphate, chloride, etc. Soil microorganisms, principally bacteria, fungi and streptomyces, possess remarkable powers for using the strange pesticidal molecules to obtain energy and raw materials for growth. Even though soil microorganisms are frequently regarded as omnivorous and biochemically omnipotent, they are often unable to destroy to significant extents many organic pesticides.

In a general sense, microorganisms in soil may influence pesticides in several ways. First, they may effect degradation with inadvertent detoxication and mineralization of a pesticide. The second effect may be that of partial or incomplete degradation with harmful or potentially hazardous substances remaining in the soil. Third, an initially nontoxic pesticide may be rendered toxic through degradation. Fourth, the rate of dissimilation may be too slow to be of any practical significance in regard to prevention of soil or water contamination. Fifth, a toxic molecule may be transformed into a product that exerts some beneficial effect upon crops, soil fauna, or microorganisms.

Shedding light on pesticide degradation in soil is an arduous undertaking. Most pesticides applied at recommended rates represent very small quantities when distributed throughout the soil mass. The concentrations of any intermediates are likely to be manifoldly smaller than that of the applied chemical, and are difficult to identify and study. The microorganisms capable of attacking most pesticidal molecules are ubiquitous. Yet, in order for the organisms to decompose a pesticide, there are at least five conditions[43] that are applicable: (1) An organism must exist in the soil and be capable of degrading the chemical; (2) The pesticide must be biodegradable; (3) The chemical must come in contact with the organism; (4) The compound must effect the synthesis of adaptive enzyme systems; and (5) Environmental conditions must be favorable for the growth and proliferation of the organism. On the basis of the limited data available, the biological detoxication of pesticides is thought to involve the following principal biochemical reactions: dealkylation, dehalogenation, hydrolysis, oxidation, reduction, ether fission, hydroxylation, ring cleavage, conjugation,[44] and cooxidation.[45]

Dealkylation

In many pesticides alkyl groups are attached to the carbon skeleton through N, O, or S linkages. The process of dealkylation during biodegradation is common with several pesticides. Generally the alkyl group of the phenoxy herbicides, for example, is cleaved off and the aromatic part of the molecule is released in soil as the corresponding phenol.[46] Using oxygen-labeled phenoxyacetic acid, it was shown that resting cells and cell-free extracts of a soil-isolated Arthrobacter sp. quantitatively oxidize this acid to oxygen-labeled phenol.[47]

The mechanism of N-dealkylation is not well understood. However, this mechanism is the major pathway in the biodegradation of s-triazine, phenylurea, dinitrotoluidine and dipyridyl herbicides.[48] Most recent information indicates that this N-dealkylation takes place through the intermediate formation of an N-hydroxylmethyl intermediate.[49] Where amines are involved the resulting N-hydroxymethylamine would be unstable and further decompose to the dealkylated amine and formaldehyde.[44]

Phenylacetamides, phosphoramides, phosphoric acid, crotonides, N,N-dimethylcarbamates, and N-methylcarbamates yield hydroxylated intermediates which are relatively stable for isolation and identification, thus providing evidence for their existence.[49]

N-dealkylation with formation of N-oxide has also been suggested as a possible mechanism.[50] The organophosphate schradan is biodegraded to the biologically active schradan oxide.[51] The occurrence of N-oxide in the metabolism during N-dealkylation is, however, very doubtful.

Dehalogenation

Dehalogenation is one of the most common mechanisms of biodegradation of pesticides in soils. It is considered to be the first reaction in the catabolism of several aliphatic acid pesticides and chlorinated hydrocarbons. Dehalogenation, for example, of dalapon by Arthrobacter sp. results in the formation of pyruvic acid, and subsequently the formation of alanine, CO_2, and presumably intermediates of the tricarboxylic acid cycle.[52] Enzymatic dehalogenation of other aliphatic acids involves a sequential breakdown by dehalogenation and hydroxylation.[53] The chlorinated hydrocarbon insecticides such as endrin, aldrin, dieldrin, heptachlor, chlordane, and DDT generally resist microbial degradation. Some microorganisms, however, can convert DDT to DDD.[54]

Hydrolysis

Soil microorganisms are also involved in hydrolytic cleavage of amide and ester linkages. These types of linkages are encountered in many pesticides. Organophosphate insecticides are most commonly encountered as phosphate esters. Even though considerable evidence is on hand showing that organophosphates are degraded by chemical hydrolysis,[55,56] several organisms have been isolated and shown to be very active in degrading malathion.[57] The degradation has been shown to occur through carboxyesteratic hydrolysis as well as by demethylation processes. The chief malathion derivatives are carboxylic acids.

Microbial hydrolysis is also believed to be the major metabolic mechanism by which phenylcarbamates and acylanilides are degraded.[44] Enzymes involved in the hydrolysis of both the phenylcarbamates and acylanilides have been isolated and identified; however, the exact site of the enzymatic cleavage (ester linkage or the amide bond of chlorpropham) has not been determined.[44] Scant evidence on the microbial dissimilation of methylcarbamates, thiocarbamates, and dithiocarbamates points to the ester linkage as the most probable site of attack. Ester hydrolysis seems to be the initial microbiological process in this degradation.[44]

Oxidation

Oxidation is another tool which soil microorganisms use to degrade pesticides. Many chlorinated hydrocarbons containing isolated double bonds are converted to their corresponding oxides by the activity of microorganisms. For example, soil microorganisms convert aldrin to dieldrin and heptachlor to heptachlor epoxide.[58] Evidence for beta oxidation of phenoxyalkanoic acids in soils has been obtained with indigenous soil populations.[59] Phenoxyalkanoic acids with a large even number of carbons in the side chain are oxidized to products with a small number of carbons. Phenoxyalkanoic acids with an uneven number of carbons in the side chain are oxidized to the corresponding valerate, propionate and phenol derivatives.[44]

Reduction

The reductive processes in the decomposition of pesticides by soil microorganisms are governed chiefly by soil aeration. Many nitro groups of pesticides are generally reduced to corresponding amines under anaerobic or semianaerobic conditions. Dealkylation of the herbicide trifluralin in aerobic soils occurs through progressive reduction of the nitro groups. This process, however, is reversed under anaerobic conditions.[60] Soil yeasts have been reported to participate in the conversion of parathion to aminoparathion in soils.[61] Many soil microorganisms have been shown to be capable of reducing pentachloronitrobenzene (PCNB) to pentochloronitroaniline at a stubstantial rate, particularly when soil was submerged in water over prolonged periods of time.[62]

Hydroxylation

Soil microorganisms also employ hydroxylation in their degradation of pesticides. This process appears to be most common with soil fungi and less common with soil bacteria and streptomyces. Many phenoxyacetic acids are hydroxylated by _Aspergillus_ _niger_ without further metabolizing the resulting hydroxy acid.[63] The same organism has been reported to both hydroxylate 2,4-D in the 5-position, and metabolize 2,4-D by hydroxylation and chlorine shift to 2,5-dichloro-4-hydroxyphenoxy acetic acid.[64] A soil bacterium is reported to be capable of metabolizing 4-chloro-2-methylphenoxyacetic acid to several products.[65]

Ring Cleavage

Ring cleavage is a quite common mechanism of degradation of many pesticides by soil microorganisms. Several phenoxyalkanoic acid herbicides are degraded to the corresponding catechols, which in turn are broken down to yield the corresponding chloromuconic acids. The mechanisms involved are probably dehalogenation and the formation of simple organic acids which are used as energy substrates by the heterogeneous soil microflora.[66] Pesticides belonging to the class of s-triazines also undergo ring cleavage by microbial action but the extent to which this occurs is not known.[67] Neither is it known what the mechanism is. Studies on the evolution of carbon dioxide from microbial systems containing s-triazines appear to indicate that microorganisms do affect the cleavage. Occurrence of ring cleavage, if at all, of s-triazines is very much dependent upon environmental conditions, including soil type, temperature, moisture level, aeration, and supplemental energy sources.[68] Ring cleavage probably occurs only after hydroxylation. Complete ring cleavage, however, is considered to be an unlikely pathway, and it is quite improbable that it is the major mechanism of s-triazine degradation in soil.

On the other hand, carbaryl, a bicyclic ring compound of methylcarbamate, is metabolized similarly to naphthalene.[69] Initially it is hydrolyzed to 1-naphthol. Subsequent reactions such as hydroxylation, ring cleavage, and decarboxylation would for all practical purposes form similar or identical products to those observed during the metabolism of naphthalene. The final products are salicylic acid and catechol. Other methylcarbamates fall in the same line of mechanisms of microbial degradation.

Conjugation

Conjugation can be visualized as a process opposite to that of degradation. While degradation implies a partial or complete breakdown of pesticide molecules, conjugation or condensation refers to coupling of the pesticidal chemical, or a portion thereof, to similar or dissimilar compounds. Conjugation or condensation plays a detoxifying role in that the union may result in the ultimate inactivation of the pesticide by blocking it from further reacting with other compounds.[44] Sacharomyces cerevosiae is reported to be involved in certain conjugation reactions.[70] It has also been observed that compounds containing -SH are converted by microorganisms to aminobutrylc acid derivatives.[70]

A conjugation type reaction occurs in the reductive metabolism of the herbicide prometryne. A number of aniline-based pesticides in soils are transformed by microorganisms to azobenzenes as major metabolites.[58] The formation of azobenzenes has been linked to peroxidase activity.[71] Only the chlorosubstituted anilines, however, form substantial amounts of azobenzene from peroxidase oxidation of substituted anilines. Better understanding of the mechanisms of conjugation must await further studies in which additional light hopefully will be shed on this subject.

Cooxidation

Recent developments on the subject of microbial degradation of pesticides strongly indicate a probably widespread mechanism-cooxidation. "Cooxidation" is described as a process in which microorganisms oxidize a compound without being able to utilize the energy derived from the oxidation.[72] It has been observed that a soil bacterium which uses 2,4-D as an energy source contains enzyme systems capable of oxidizing other phenoxy compounds. However, these compounds do not support the growth and proliferation of the bacterium.[45] Similarly, many organisms degrade organophosphates without being able to avail themselves of the carbon or phosphorus sources, at least not to a significant degree.[73] Cooxidation is thought to account for the breakdown of many pesticides which do not support microbial growth to any degree. It is even suggested that cooxidation may be utilized for enhancing the rate of dissimilation of some recalcitrant pesticides. In such situations a biodegradable similant for a resistant pesticide could be added to the soil to stimulate substantial build up of microbial populations possessing the appropriate degradative enzymes for both the fake and the refractory pesticide and thereby bring about a greater rate of degradation of the persistent compound.

Biodegradation of Mixtures of Pesticides

Under most environmental conditions no pesticide would be expected to occur as a single toxicant but rather as a mixture of pesticides. The mixtures may not only be made up of different compounds within the same class of pesticides, but they will also be made up of compounds belonging to different classes. In a general sense several herbicides, insecticides, fungicides, and nematocides may occur in close proximity to each other in the field in a single growing season. Logically, interactions may be expected not only among the pesticides themselves, but also among the pesticides and their intermediates and among both pesticides and intermediates and growing plants. In fact, interactions in terms of plant response have been observed for herbicide mixtures, herbicide-insecticide mixtures, and for fungicide-herbicide mixtures.[74] The effects of these interactions are both favorable and unfavorable, in that they either increase or decrease phytotoxicity of pesticides toward target or non-target organisms. For example, in one investigation the microbial degradation of the herbicide dalapon was found to be suppressed in the presence of the second herbicide, amitrole. However, if the soil contains a dalapon-enriched soil population, the effects of amitrole are substantially decreased. Numerous other examples could be cited, but this would only further inflate this already somewhat lengthy coverage of the microbiological processes as they relate to the fate of pesticides in soils.

Undisputably the practical importance of such information is very great. The microbial degradation and metabolism of sole toxicants, as presented in the foregoing discussion, would be extremely difficult to fit into situations where combinations of pesticides may exist. However, it is imperative for us to understand the degradative mechanisms of pesticides and products of pesticides as they occur in natural soils in order to prevent or minimize contamination of our environment. So far, field and laboratory experiments appear to indicate quite clearly that both the longevity and toxicity of individual pesticides in the soil may change in the presence of other pesticides.[44] Therefore, in most cases information is badly needed specifically on the behavior and fate of formulated pesticides.

It should be reemphasized that the foregoing consideration of microbial degradation of pesticides is but a very sketchy survey of existing information. Considerably more information exists, but it is far from a complete body of knowledge. It is mandatory that the agents of detoxifications of pesticides be known, the environmental factors influencing the rate of breakdown understood, and the possible combinations of pesticide materials be on inventory in order to permit the careful control and management of environmental pollution by pesticides and their degradation products. Finally, new approaches in the use of pesticides must be sought where equally effective, but less recalcitrant, materials can be used instead of the highly resistant ones presently in use.

VOLATILIZATION OF PESTICIDES FROM SOIL SURFACES

One of the ways in which pesticides "disappear" from soil is by volatilization from the soil surface. In this case, however, the parent compound or its metabolites have not really disappeared. They have only been transported into the air where they will be subject to photolysis by sunlight. There are several factors which affect volatilization of pesticides.

Loss of a pesticide by volatilization is a function of the water solubility and vapor pressure of the compound.[75] The higher the vapor pressure the greater the degree of volatility at a given temperature. Since the vapor pressure of an organic molecule is temperature dependent (increases with increasing temperatures), higher temperatures affect greater losses of pesticide by evaporation. For example, after 5 months weight losses of dieldrin from aluminum disks at 30, 35, and 40°C are 6, 12, and 40%, respectively, while corresponding DDT losses are 7, 9, and 12%, respectively.[76]

Pesticide vaporization is also dependent upon the concentration of pesticide material present in the soil.[77] At constant soil water content and constant temperature the vapor densities of dieldrin and lindane increase with concentration and reach a saturated vapor density equal to that of the insecticide without soil at concentrations near 25 ppm for dieldrin and 55 ppm for lindane. This relatively low soil concentration needed for a saturated vapor indicates that these pesticides will be subject to relatively high rates of loss by volatilization.[77]

The presence of organic matter and clays in soil also affects evaporative losses of pesticides. For example, at the wet and dry extremes of soil water levels vaporization losses of dieldrin are inversely proportional to soil organic matter content but are not affected by clay contents. This indicates that clay plays only a minor role in the adsorption of nonpolar compounds.

Perhaps the most important influence on volatilization of pesticides is the soil moisture content. Soil water content does not affect the vapor density of either dieldrin or lindane until its content decreases below that equivalent to one molecular layer of water.[77] Then the vapor densities drop to very low values. Thus, the soil is extremely dry before the vapor density decreases appreciably. Moreover, the effect of soil moisture content on volatilization of pesticides appears to be reversible. This very marked effect of small amounts of water on vapor density of pesticides such as lindane and dieldrin in the dry soil range would explain their greater volatilization from wet than from dry soils. Apparently, increasing the water content of soil increases the vapor density, and thus the volatility, of the pesticide because the water competes with the pesticide for adsorption sites on the soil.[77]

Further support is lent to this conclusion by a study of the actual rate of volatilization of dieldrin as related to soil water content.[78] Volatilization of dieldrin occurs at a rapid, almost constant rate until the soil becomes very dry due to evaporation of water. When the water loss becomes insignificant in the dry soil, dieldrin loss also becomes insignificant due to reduced vapor density caused by adsorption of dieldrin on the dry soil. The almost constant rate of volatilization of dieldrin at varying soil water contents indicates that its volatility is not enhanced by evaporation of water from the soil. In other words, water loss, per se, does not increase the rate of volatilization by codistillation.[78]

Loss of pesticides with which water can compete for adsorption sites appears to be dependent on the time required for the soil to dry enough to reduce the vapor density of the pesticide to an insignificantly low value. Moreover, this method of loss may be a major pathway for loss of relatively nonvolatile pesticides from soil.

MOVEMENT OF PESTICIDES IN SOIL

After application to the soil surface, pesticides may be transported from the original site of application by movement along the surface of the ground or by entrance into the soil. On the surface the pesticides may bind to or be adsorbed by the soil particles and thus be carried away in the runoff water when these particles are eroded. In this manner pesticides contaminate our lakes, rivers, and streams. Pesticides enter the soil by diffusion of vapor into the airspaces of the soil or by movement into the soil via the soil water.[7]

Movement by diffusion through the soil airspaces is important for those pesticides with a high vapor pressure, i.e. soil fumigants and is probably more important than downward water flow for transport of these pesticides. Soil porosity[79] and pore size and continuity[80] appear to be the most important factors influencing this mode of movement.

The downward carrying of pesticides in the percolating water of the soil appears to be the principal means of movement of the relatively nonvolatile pesticides.[7] This type of movement, which is known as leaching, is affected by the physical and chemical properties of both soil and pesticide as well as by the climate.

The movement of pesticides in the soil as related to the physical-chemical properties of the soil and pesticide appears to be the function of the relative effects of several factors.[7] One of these is irreversible adsorption. In this case the adsorbed pesticide cannot be leached because it is bound to the soil. However, if the pesticide is reversibly adsorbed, it can be leached from the soil upon desorption. Chemical reactions of pesticides with soil constituents (i.e., chelation and precipitation reactions) decrease the extent of pesticide movement. Pore size and distribution as well as soil texture also affect leaching. Pesticides will be removed more rapidly from soil containing a high portion of large pores which are fairly evenly distributed than from soil which contains a large portion of small pores. Moreover, pesticides are leached to a greater degree from light-textured soils such as sand than from heavier-textured soils. The entrance of the pesticide into solution in the soil water increases the pesticide movement because in general water soluble pesticides are leached much more extensively than insoluble ones. The extent of leaching is directly proportional to both the soil moisture content and the rate of flow of water through the soil.

The most important climatic factor influencing pesticide movement in soil is rainfall. The total amount, the intensity, and the frequency of rainfall all appear to affect movement.[7] For a given compound on a given soil type, increasing the amount and the frequency of rainfall increases the amount of pesticide leached. Moreover, the pesticide is leached to greater depths under these conditions.[81,82] However, the converse appears to hold true for rainfall intensity. For example, monuron is leached to greater depths under low rainfall intensities.[83]

Most pesticides that enter the soil are moved to some extent by the percolating soil water. This movement can be advantageous in that distribution of a pesticide through the soil increases its chances for chemical or microbiological degradation. However, the presence of pesticides in soil water can also create water pollution problems by entrance of the pesticides into the ground water and subsequently into lakes, rivers, and streams.

PESTICIDES IN CROPS

It would be an almost impossible task to attempt to present within the framework of this paper a discussion on the subject of pesticides in crops which would even remotely resemble a comprehensive treatise. In the space and time allotted, only certain principles that have been developed from research on the penetration, adsorption, translocation, mechanisms and sites of action, and metabolism of pesticides in plants can be discussed.

Foliar distribution, retention, and uptake of pesticides is greatly influenced by plant form, leaf shape, leaf position, leaf density, leaf surface, and margins. Plants that grow erect, spreading, or prostrate display different pesticide-recipient characteristics and retention-capacity patterns. Broad, large, narrow, short, or linear leaf shapes enhance pesticide reception, distribution, and retention patterns. On the other hand, upright, horizontal, or pendulous leaves which form foliage canopies of varied densities also influence retention and uptake of pesticides. Furthermore, leaves with waxy, hairy, or different sculptured leaf surfaces absorb and retain pesticides differently.

The amount of pesticide material which enters the cell is probably determined by the number and pattern of distribution of stomates, as well as by the nature of the cuticle. Additionally, the form, shape, size, density, distribution, and other characteristics of roots in relation to applied pesticides influence, to a degree, the amount of pesticides that come in contact with the plant.[84]

One of the most studied processes is the absorption or translocation of pesticides in plants, particularly the absorption of herbicides. This translocation is influenced by the same factors that influence plant growth in general and the transport of inorganic and organic solutes. Pesticides which are taken up by the plants may also be immobilized in the tissue by either adsorption to, or conjugation with, cell constituents. The translocation of pesticides depends upon the kind of pesticide and upon the plant species. For example, certain grasses may impair the translocation of applied pesticides by the intercalary meristem. In addition, certain herbaceous and woody plants may present "certain road-blocks" to translocation. This interference with the translocation may often prevent pesticides from reaching their site of action (many herbicides fall in this category). Compounds having very low solubilities in water generally would not be translocated in plants to any appreciable extent. However, this trend does not hold true at all times since BHC (a low solubility compound) was found to translocate from soil to carrot fibrous roots, edible part, stems, and leaves.[85] Heptachlor also appears to be translocated since studies have shown the presence of this compound in the aerial parts of plants grown in soil to which heptachlor was applied.[86] Similar observations have been reported with strawberries and other crops grown in soils treated with aldrin, dieldrin, lindane, or heptachlor.[87,88,89] There is evidence of substantial absorption of pesticides by crops from soils previously treated with pesticides. This appears to be particularly true where short-term crops are raised, such as in truck farming, and where repeated applications of pesticides may be used for each crop.[90]

Many pesticides are conspicuous in their capabilities to modify and control plant growth by inhibiting key metabolic processes or by creating obstacles for the biosynthesis of metabolites indispensible to plant growth.[84] For example, some herbicides cause starvation to death of plant cells by blocking photosynthesis, while others may uncouple oxidative phosphorylation and thereby prevent many of the biosynthetic reactions from taking place in the cells. Many plant enzyme systems may also become victims of the herbicide activity and be deactivated. In addition to the inhibition of purely biochemical processes, physical effects of pesticides may also disrupt the normal physiological functions of the highly organized plant cellular components.

The ability of plants to metabolize pesticides which have been applied either to the surface of the plants or which may be present in the soil may serve as a means of reducing the persistence of the pesticides in the environment. The destruction of organophosphate insecticides by hydrolysis on plant surfaces and within plant cells (especially for systemic insecticides) is a good example of safe use of such very toxic pesticides as TEPP, phosdrin, and mevinphos on edible fruits and vegetables within a day or two of harvest.[90] Hard pesticides (chlorinated hydrocarbon insecticides), on the other hand, do not undergo degradative reactions in such short periods. Other studies have shown that simazine, a pre-emergence herbicide used for weed control in corn is converted to a nonphytotoxic form when taken up by the roots of the corn plant. Thus, corn is tolerant to simazine while many weeds, incapable of metabolizing simazine, are readily injured and controlled.[84] Simazine is found to inhibit photosynthesis. However, by feeding a source of readily available carbohydrate, such as glucose, to the affected plants, it is possible to protect the plants against the phytotoxic effects of this herbicide.[91] Similar results have been obtained with some of the phenylurea herbicides.[84]

Several chloro-aliphatic acids (particularly dalapon) inhibit the synthesis of pantothenic acid (vitamin B) in plants. However, feeding pantothenic acid to barley plants through their leaves partly prevents this inhibitory effect of dalapon on plants.[92] Changes in concentration of certain pesticides may also have different effects on plants. For example, low concentrations of the N-phenylcarbamate herbicides stimulate respiration in root tips of exposed plants, whereas higher concentrations markedly decrease respiration.[93]

Plants differ in their capacity to beta-oxidize the long side chains of chlorinated phenoxyalkylcarboxylic acids. Certain long-chain pesticides are non-phytotoxic unless the plant can degrade the side chain to yield the corresponding acetic acid derivative.[94]

Many pesticides are absorbed by plants at sites not involved in the growth response. The resistance of plants to 2-methyl-4-chlorophenoxyacetic acid (MCPA) is due principally to tying this compound to plant materials not involved in growth.[95]

Numerous other examples could be cited regarding the metabolism of pesticides in plants. It can be generalized that any organic pesticide introduced into a plant may undergo degradation, modification of structure, or condensation with natural plant constituents. The selective action of pesticides may be due to differential absorption, translocation, and the rate at which various species accomplish detoxification through complete breakdown. Often a detoxification mechanism may consist in a simple conjugation of pesticides with carbohydrates, proteins, amino acids, etc. In general the translocation of toxic chemicals throughout the plant depends upon complex and interrelated morphological, physiological, biochemical, and physical factors. There are, however, many unknown factors. For example, some pesticides are applied in one form, translocated in a changed form, and are inhibitory in still another form. Many other chemicals, however, remain unchanged.

SUMMARY AND CONCLUSIONS

In order to feed and clothe the increasing population of our earth, man is compelled to use pesticides. At the same time he must be aware of the fate of these toxic materials in his environment, particularly in regard to relation of that fate to his own well-being. Investigations of pesticides in soils generally have either been concerned with the physico-chemical aspects of soil-pesticide relationships or have been strictly microbiological in nature. From these diverse studies man has learned that adsorption, chemical and photochemical reactions, microbial action, volatilization, leaching, and plant uptake are key processes which influence the fate of pesticides in the soil. However, much of the work has been limited in scope and qualitative in nature, and much more effort must be expended to obtain a complete understanding of the behavior of pesticides in soil.

Adsorptioh of pesticides on soil particles is one of the more important of the deactivating mechanisms because it influences all the others. Adsorption studies have indicated that certain soil components such as clay and organic matter are involved, but no attempt has been made to quantitatively measure the relative importance of these components. Moreover, there is little information pertaining to the influence of the chemical nature of the pesticide on adsorption. Quantitative information about these phenomena as well as about the effects of pesticide adsorption by soils on the mineral element absorption by plants is needed.

Chemical decomposition in the soil and photochemical degradation on the surface are the two major nonbiological methods of pesticide degradation. However, the degradation products resulting from these decompositions are often identical to those resulting from microbial degradation, and it is difficult to determine the chemical and photochemical behavior of pesticides in soil. Consequently, much of the knowledge pertaining to the chemistry and photolysis of pesticides has been gained from the test tube rather than from the soil.

Of all of the modes of pesticide detoxification in soil, the most important is microbial degradation. As soil conditions become more favorable to microbial activity, the rate of pesticide decomposition increases. Most of the microbiological investigations have been concerned with isolation of microorganisms capable of degrading specific pesticides in pure cultures and determination of the effects of pesticides on the total microbial population and on specific microbiological processes which occur in soil. However, basic investigations into the biochemical aspects of microbial degradation are urgently needed. If one knew what specific structural linkages were broken in the chemical molecules, perhaps he could synthesize pesticides which could be degraded by soil microorganisms without the risk of residue.

Information is also lacking on the volatilization characteristics of pesticides. As has been shown elsewhere in this paper, even some of the most persistent pesticides such as dieldrin and lindane are appreciably volatilized from soil except under extremely dry conditions. Therefore, an understanding of the factors influencing volatility might enable man to produce pesticides with tailor-made periods of persistence.

Movement of pesticides in soils is not fully understood. Numerous studies have shown that pesticide movement is dependent on, or influenced by, the physical and chemical properties of both soil and pesticide. However, the interactions of these properties are not known and should be investigated.

Plant absorption of pesticides is one of the primary means by which pesticide residues enter our food chain. While much information pertaining to the absorption and translocation of phytotoxic pesticides such as herbicides, growth regulators, and defoliants by plants has been accumulated, the knowledge about absorption and translocation of nonphytotoxic pesticides (insecticides, fungicides, and nematocides) is inadequate. Since plants are the primary source of food, it is imperative that this information be known.

As new pesticides are developed, their fate and behavior in soils and plants must be assessed in relation to all of these factors before they are released to farmers of home owners for use. This method is one of few ways to avoid the presence of harmful residues in soil, water, plants, and ultimately in our food supply.

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SAFETY IN HANDLING PESTICIDES

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In any given year, a number of people become ill or die as a result of overexposure to pesticides. The circumstances of the exposure may include among others a child who finds a pesticide improperly stored or used and eats or drinks it, or, a workman in a formulating plant or a farmer who accidently spills a pesticide on himself and does not take the necessary action to decontaminate himself and seek medical aid. Regardless of the circumstances, most of the illness and many of the deaths associated with pesticide products could have been avoided.

The watchword is "use common sense" when handling any toxic material such as pesticides. Pesticides are designed for a specific task--namely, to kill. They do not discriminate in whom or what they kill. Regardless of the manner of exposure -- controlled, chronic, or sudden and accidental -- their action remains the same.

In considering safety in manufacture, formulation and application, attention is focused on minimizing worker hazard and preserving the integrity of the environment. It is under the conditions of manufacture and formulation that there is the most constant danger of exposure to concentrated materials, making it imperative that safe handling practices be followed.

Both direct and indirect methods are available for insuring worker safety. Indirect methods include:

(1) Education - A worker who understands the dangers of pesticides will more readily recognize the importance of the various recommendations for precautions. By following these, he can do much to insure his own safety and the safety of others. Every effort should be made to acquaint the worker with details about those product(s) with which he works, especially the toxicity, routes of absorption, and the signs and symptoms which might develop with intoxication. He should also be instructed to seek medical aid whenever overexposure to a pesticide is suspected without waiting for the development of severe illness.

(2) Personal Hygiene - The importance of personal hygiene should be stressed. This includes washing of hands (and face when needed) before eating or smoking and showering at the end of work each day. (Some workers may have to be taught the proper way to shower.) Clean work clothes and underwear should be worn daily.

(3) Medical Supervision - An indirect method of insuring worker safety is a program of medical supervision. Periodic testing of blood cholinesterase activity and/or metabolite excretion will indicate the worker who is experiencing unusually heavy absorption through chronic overexposure or sloppy work habits and who as a result is in danger of developing a toxic illness.

Direct methods, which physically prevent exposure are usually various types of protective devices and clothing.

The three routes of entry of pesticides into the body -- dermal, respiratory and oral, are all important to the worker. The dermal route of exposure is the most significant to workers involved in the manufacture, formulation or application of pesticides. Wolfe[1] and his co-workers showed in a study of several hundred pesticide applicators that over 97% of the pesticide to which the body was subjected was deposited on the skin. This was especially true of applicators of liquid sprays. The importance then of protecting the body surface from contamination is obvious.

Factors such as fatigue, carelessness, boredom with the routine nature of many plant operations, and the sheer bulk of many of the pesticidal product elements to gross contamination of workers and their working environment resulting from spills, or the dusty nature of the work.

Recent work by Maibach and Feldman[2] in California showed that pesticides are more readily absorbed in some body areas than others. Using parathion as a representative compound, these investigators found almost 100% absorption in the scrotal area. Saturation of the skin in the scrotal area of parathion or other substances well absorbed across the intact skin through spillage or saturation by sprays would be akin to an injection of the material directly into the vein as far as absorption is concerned.

While cloth provides some degree of protection, waterproof trousers are recommended for protection. A waterproof apron would be the second choice. Daily changes to clean clothing and daily shower are both important adjuncts to direct protection of the lower body area.

While absorption is somewhat less efficient over the upper body, this area still has great exposure potential. A waterproof jacket or raincoat with long sleeves and a close fitting neck should be used giving protection to the upper back, shoulders and forearms of workers.

The worker's comfort should be considered. In hot weather, protective gear will become unbearably hot. By late morning, our fully protected worker can be seen in T-shirt and baseball cap. What should be encouraged under these conditions is at least minimal protection by long sleeve cotton shirts which are laundered after each day's use and changed when they become wet with spray. This should never be considered adequate protection.

Light colored garments of protective clothing can be as much as 8°- 10°F. cooler than the familiar black or dark green ones.

In the area of the head and neck, Maibach, et al found absorption of parathion was 32 to 47% of the applied dose.[2]

Headgear with a bill or brim will give some protection to the scalp, face and neck area. A waterproof hat with a wide brim is available that affords good protection to this area of the body.

Goggles and respirators provide considerable protection to the fact area but should be properly cleaned, serviced and stored.

The high potential exposure to the hands emphasizes the need for wearing gloves. Cloth-type gloves are not recommended as they can become soaked with pesticides and then enhance - not prevent - exposure. Rubber gauntlet-type gloves provide the best protection. The gauntlet should cover the wrist, and the glove can be turned out for easy cleaning.

Waterproof shoes or boots provide the best protection for the feet. The trouser leg should be worn outside the boot or shoe top to prevent runoff from going into the boot. Leather work boots become dried and crack when repeatedly soaked with pesticide liquids; this makes them unacceptable as protective gear when handling toxic materials such as pesticides.

Adequate respiratory protection for most types of application is provided by the use of cartridge-type respirators. In some instances, such as manufacture or formulation of extremely toxic products, self-contained or supplied-air type breathing apparatus is used. The oral route of exposure probably is not one of major concern in occupational exposure. It is usually difficult to make a clear distinction between oral exposure and respiratory exposure. Few workers would intentionally eat these products with which they work. Pesticide residues may be on the hands and transferred to lunch or snack items. Therefore, washing before eating and smoking is the best prevention for this type of exposure.

Let us now consider the safe handling of pesticides in other important areas--transportation and storage.

Pesticides may be shipped as the technical material - usually this is the undiluted chemical of up to 95% pure material - or as formulations which are mixtures in which the technical material is combined with a carrier or solvent permitting conventional application.

Hazards in the event of a spill in transit, occur through the same mechanisms as those considered earlier. That is, they may be absorbed, inhaled or ingested. This may occur through contamination of items which are coshipped or during the cleanup process. Ingestion may occur if contaminated foodstuffs are allowed to reach consumers. Pesticides cannot be shipped with foodstuffs unless they are packaged in air-tight wrappings. Unfortunately this regulation is sometimes ignored or wrappings break and the danger of secondary poisoning still exists.

Cleanup involving pesticides should be performed only by authorized persons. These persons should use adequate measures to protect themselves in the situation including measures discussed above.

The National Agricultural Chemicals Association has formed a network of safety teams to minimize the risk of injury from the accidental spillage or leakage of pesticides.

This network became operational in March of 1970. By contacting a central telephone number (513 961-4300), the team network insures that expert help will be dispatched to the scene of an accident. The safety team network furnishes personnel, equipment and expertise, to insure prompt, efficient cleanup and decontamination following major accidents involving pesticides.

The danger of fire in warehousing pesticides is a major public health hazard. Fires involving pesticides are expecially hazardous because of the possibility of poisoning from vaporized chemicals added to the usual fire hazards of smoke inhalation and thermal burns. Containers of pesticides rupture. Water and chemicals used to fight the fire spread contaminants over a wide area. Heat and air currents combine to vaporize pesticides and cause them to enter the air. Fire fighters must take extraordinary precautions to avoid breathing fumes and smoke from ignited storage areas and avoid body contact with water and debris.

To repeat -- safe handling practices relating to pesticides are matters of common sense.

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PESTICIDE REGULATION

Emerson R. Baker, J. D.

Introduction

For the purposes of this summary, the laws and regulations governing pesticides have been divided into two main groups, based upon the source of the law, viz: Federal and State.

Another equally valid division could be made according to what is to be regulated, viz: first, the pesticide chemical itself, its chemistry, toxicity, and labeling, and second, regulation of the person who uses the pesticide. The laws governing the groups resulting from this type of division are the familiar "registration and labeling laws," and the "use and application laws."

Reorganization of Federal Pesticide Control Responsibilities

In discussing Federal pesticide control legislation, mention should be made of Reorganization Plan No. 3, of 1970 (submitted to Congress by President Nixon on July 9, 1970) which established the Environmental Protection Agency (E.P.A.) as a separate organizational unit in the Federal Government, effective December 2, 1970.[1]

This reorganization did not produce new pesticide control laws, but it did bring together under one roof, some or all legal functions of certain agencies or departments of the government relating to pesticide control (and other environmentally harmful substances or practices).

The reorganization plan (which has the effect of law) states, in part "...there are hereby transferred to the Administrator (E.P.A.):

> "(1) all functions vested by law in the Secretary of Interior and the Department of Interior which are administered through the Federal Water Quality Administration...
>
> "(2) functions vested in the Secretary of Interior... (relating to studies on the effects of insecticides, herbicides, fungicides, and pesticides upon the fish and wildlife resources of the United States)[2]

"(4) the functions vested in the Secretary of Health, Education, and Welfare of establishing tolerances for pesticide chemicals under the Federal Food, Drug, and Cosmetics Act...

"(8) (i) The functions of the Secretary of Agriculture under the Federal Insecticide, Fungicide, and Rodenticide Act..."

A pesticides office within the agency has been established with the Director reporting directly to the Administrator. [3]

This office is responsible for all pesticides activities of the agency, including:

(1) establishment of tolerance levels for pesticide residues which occur in or on food

(2) registration of pesticide uses for protection of human safety

(3) monitoring of pesticide residue levels in food and portions of the enfironment

(4) review of pesticide formulations for efficacy and hazards

(5) regulation of sale or use patterns when necessary

(6) checking for compliance with label provisions

(7) research on effects on human health, non-target fish and wildlife and their environments, and,

(8) establishment of guidelines and standards for analytical methods of residue detection.

While each Federal pesticide control law retains its legal identity, the administration of all pesticide laws are now in one agency (some research and related pesticide investigations will still be carried out by other Federal agencies and some agencies have regulations relating, in part, to pesticides).

It should be kept in mind that a pesticide control law may be but a small part of a more comprehensive law relating to a broad subject, or added as an amendment to existing legislation (e.g., The Miller Amendment to the Federal Food, Drug, and Cosmetic Act).

Federal Laws

Federal Insecticide, Fungicide, and Rodenticide Act.[4]

The Federal Insecticide, Fungicide, and Rodenticide Act of 1947 (FIFRA) replaced and expanded the Insecticide Act of 1910.[5] The old act regulated insecticides and fugnicides only and at a time when such products were comparatively simple, consisting mainly of Paris green, pyrethrum, bordeaux mixtures, and like products.

The purpose of the law is to regulate the marketing of economic poisons and devices by means of a registration and labeling procedure which requires producers to present evidence of the safety of these products when used as directed and their effectiveness for the purpose claimed on the label.

In applying for registration of a pesticide, the applicant must furnish:

"(1) the name and address of the registrant and the name and address of the person whose name will appear on the label, if other than the registrant;

(2) the name of the economic poison;

(3) a complete copy of the labeling accompanying the economic poison and a statement of all claims to be made for it, including the directions for use; and

(4) if requested by the Secretary, a full description of the tests made and the results thereof upon which the claims are based."

"b. The Secretary, ... may require the submission of the complete formula of the economic poison. If it appears...that the composition of the article...and its labeling and other material required to be submitted comply with the requirements of section 3 of this Act, he shall register it."

The Act prohibits shipment in interstate commerce of products which are not registered or are adulterated or misbranded. Products found in violation of the Act may be seized and criminal action instituted against the producer.

In 1959, the Act was amended[6] and updated to include nematocides, plant regulators, defoliants, and desiccants as economic poisons. Poisons and repellents used against amphibians, reptiles, birds, fish, mamals, and invertebrates, are, by regulation, classed as economic poisons.[7]

A 1964 amendment [8] eliminated a controversial "registration under protest" section which had permitted marketing of an unregistered pesticide pending the outcome of full investigation of its usefulness.

Until December 2, 1970, the Act was administered by the Director of the Pesticides Regulation Division, Agricultural Research Service, USDA. The Pesticide Regulation Division also issued interpretations with respect to certain of the more troublesome regulations, e.g., claims for safety and non-toxicity, warning and caution statements, labels for large containers, directions for use, etc.

This law is now administered by the Environmental Protection Agency under the authority of Reorganization Plan No. 3 of 1970.

Federal Food, Drug, and Cosmetic Act of 1938.[9]

The Federal Food, Drug, and Cosmetic Act of 1938 (FFDCA)[10] which provides for the regulatory activities of the Food and Drug Administration concerned with foods, drugs, devices, and cosmetics, did not cover pesticides as a separate subject of regulation at the time of its enactment.

In 1954 the FFDCA was amended[11] to require regulation of pesticide chemicals in or on raw agricultural commodities shipped in interstate commerce.

The amendment provides that "any...pesticide chemical...added to a raw agricultural commodity, shall be deemed unsafe...unless--

> "(1) a tolerance for such pesticide chemical... has been prescribed, or
>
> "(2) the pesticide chemical has been exempted from the requirement of a tolerance...

The amendment also provides that the Secretary of Agriculture shall certify to the Secretary HEW that the pesticide chemical is useful for the purpose for which a tolerance or exemption is sought, (or that the applicant requesting certification shall be told that the pesticide chemical does not appear to be useful for the intended purpose.)

In requesting the establishment of a tolerance, the manufacturer is required to furnish data showing:

(a) the name, chemical identity, and composition of the pesticide chemical;

(b) the amount, frequency, and time of application of the pesticide;

(c) full reports of investigations made with respect to the safety of the pesticide;

(d) the results of tests on the amount of residue remaining, including a description of the analytical methods used;

(e) practicable methods for removing residues which exceeds any proposed tolerances;

(f) proposed tolerances for the pesticide (if tolerances are proposed), and;

(g) reasonable grounds in support of the petition.

The FFDCA also provides that "...a raw agricultural commodity... bearing or containing a pesticide chemical applied after harvest [is misbranded]... unless the shipping container bears labeling which declares the presence of such chemical ... the common or used name and the function of such chemical...".

Federal Water Pollution Control Act (1948)[12]

Federal Water Pollution Control Act (1948), as amended, relates to pollutants, including pesticides, in water and waterways. It was originally administered by the Surgeon General of the Public Health Service but was transferred to the Secretary of the Interior effective May 10, 1966.[13] One of its objectives was to encourage enactment of uniform state laws to prevent water pollution. It is interesting to note that Federal legislation as early as 1899[14] had made it unlawful to deposit refuse matter of any kind, other than that flowing from streets or sewers in a liquid state, into any navigable waters or its tributaries, unless a permit for such disposal had been obtained from the U. S. Corps of Engineers. The law, mostly dormant since its inception, is now being implemented through a permit system.[15]

Since December 2, 1970 all authorities of the Federal Water Pollution Control Act are administered by the Environmental Protection Agency.

Federal Regulations

Extensive regulations have been issued by the Food and Drug Administration, the Department of Agriculture, and the Federal Water Quality Administration to implement the administration of the three above listed laws.

Additionally, regulations have been issued by other Federal agencies under their basic authorities which relate in part but not exclusively, to pesticides.

Department of Transportation (DOT) [16]

Four agencies of this Department are concerned with and have statutory responsibility for the safe transportation of hazardous materials in interstate commerce.

Within the DOT is a Hazardous Materials Regulation Board which consists of the Administrator(s) of Aviation, Highway, Railroad, Coast Guard, and the Department's Assistant Secretary for Research and Technology.

It is within their authority to promulgate reasonable regulations to assure safety in transporting dangerous articles or substances in interstate and foreign commerce. Additionally these agencies within the DOT may issue regulations of their own which relate to their statutory responsibilities. Pesticides are only one of many such materials and for purposes of regulation most all are included in "Class B" poisons. Regulations are very specific concerning shipping containers, labels, and the handling of pesticides.

The Federal Aviation Agency has issued regulations[17] relating to agricultural aircraft operations, including tests of pilots regarding their knowledge of dispensing of agricultural materials or chemicals.

Among other things the test may include:

" (i) steps to be taken before starting operations, including survey of the area to be worked;

" (ii) safe handling of economic poisons and the proper disposal of used containers for those poisons;

"(iii) the general effects of economic poisons and agricultural chemicals on plants, animals, and persons, with emphasis on those normally used in the areas of intended operations; and the precautions to be observed in using poisons and chemicals;

"(iv) primary symptoms of poisoning of persons from economic poisons, the appropriate emergency measures to be taken, and the location of poison control centers..."

Additionally, the holder of a commercial agricultural aircraft operator certificate "shall maintain and keep current, at the home base of operations designated in his application, the following records:

"(1) the name and address of each person for whom agricultural aircraft services were provided;

"(2) the date of the service;

"(3) the name and quantity of the material dispensed for each operation conducted; and

"(4) the name, address, and certificate number of each pilot used in agricultural aircraft operations and the date that pilot met the knowledge and skill requirements of sec. 137.19 (e)..." (the test referred to above).

The Federal Trade Commission, organized as an independent administrative agency in 1915, is charged with keeping competition both free and fair. As part of their responsibilities, they regulate the advertising of economic poisons and generally prohibit any advertising which "contradicts, negates, detracts from, or is inconsistent with any statement, warning, or direction for use, in the labeling of such product..."[18]

They have proposed, but not yet adopted, a proposed warning statement for all economic poisons stating "...this product can be injurious to health; read the entire label carefully and use only as directed."

Executive departments and agencies of the Federal Government are required to publish their regulations and the Code of Federal Regulations has been established to accomplish this statutory requirement. The code books are revised as of January 1 each year and kept up to immediate date by daily issues of the Federal Register, in which all new or amended regulations are promulgated. Hence, to find any specific tolerance or exemptions from a tolerance for any particular pesticide in or on a raw agricultural commodity, it would be necessary to look in the current Code of Federal Regulations (Title 21 - Food and Drugs, Chapter 1, Subchapter B, Part 120) and then to check the daily issues of the Federal Register for changes (these contain cumulative indices by both subject matter and sections affected).

State Laws and Regulations

State pesticide control laws may be divided arbitrarily into the two following groups:

Registration Laws

Those which regulate the production and marketing of pesticides by requiring compliance with registration and labeling criteria prior to interstate or intrastate shipment. These are often referred to as "economic poison laws" or "insecticide, fungicide, and rodenticide acts."

Following the adoption of the Federal Insecticide, Fungicide, and Rodenticide Act in 1947, many States enacted similar legislation requiring registration and labeling of economic poisons as a prerequisite to their lawful introduction and shipment in commerce. As a result, all except two States now have pesticide registration laws, although not all States have fully implemented the authority granted. Some States exempt pesticides which have been registered under the Federal Insecticide, Fungicide, and Rodenticide Act.

The registration laws which are fully operative are considered "uniform" acts and a comparative study would show little difference in content and objectivity.

The Council of State Governments has developed a model State insecticide, fungicide, and rodenticide act which incorporated the 1959 and 1964 amendments to the Federal Insecticide, Fungicide, and Rodenticide Act, together with suggested regulations for its administration and enforcement.

Use and Application Laws

Those which:

(1) require examination and licensing of persons engaging in the business of applying pesticides (e.g., custom applicators, structural pest control operators, certain sanitation services, equipment operators, etc.).

(2) regulate professions concerned with the use and application of pesticides including consultation services and recommendations for treatment; (e.q., entomologists, plant pathologists, horticulturists, tree surgeons, etc.).

(3) (a) prohibit or restrict the use of certain pesticides.

(b) require (i) the purchaser to obtain a permit before using highly toxic pesticides (usually a written "prescription") giving the kind of pesticide to use, the concentration permitted, the crop to be treated, method of application, and precautions to be observed, and (ii) dealers in "prescription" pesticides to be licensed.

Of the various categories of State pesticide use and application laws, probably the structural pest control laws are the most uniform, and those which relate to the use and application of agricultural pesticides, the least uniform. Unfortunately, the "model" use and application acts prepared by concerned groups have followed, rather than preceded, enactment of legislation in this field.

Use and application laws generally establish qualifications for applicants; they may require both oral and written examinations; establish fees; provide for issuance, renewal, and cancellation of licenses; and grant reciprocity to non residents meeting standards equal to those of the licensing State.

Applicators are required to be financially responsible for the consequences of their acts and, to this end, a liability insurance policy or its equivalent, is a prerequisite to issuance of a license

In the model "custom application of pesticides act" prepared by the Association of American Pesticide Control Officials and published in the 1971 program of Suggested State Legislation by the Council of State Governments and in a similar model of the Food and Drug Administration, the Commissioner of Agriculture, Pesticide Control Board, or other official responsible for administration of the law, is generally given statutory authority to:

1. issue regulations
2. enforce the act
3. delegate duties
4. prescribe, restrict, or prohibit methods or materials

5. inspect premises
6. inspect equipment
7. require records or reports
8. cooperate with other agencies
9. publish information
10. conduct training courses
11. regulate storage, transportation, or disposal of pesticides or pesticide containers
12. require compliance with label directions
13. license equipment
14. subpoena persons or records
15. require filing reports of loss
16. investigate damages

Provision is made for a pesticides board in order to give representation to all groups who have a legitimate interest in controlling the use and application of pesticides. In the past, some boards have been of an advisory nature only, but more recent legislation grants the boards considerable regulatory authority, including the power to either issue rules and regulations governing pesticide use and application, or to approve them before they become effective.

Twenty States have pesticide boards, but the authority membership, and representation vary considerably from State to State.

The use and application laws have generally exempted individuals and governmental bodies who apply pesticides for their own use, however recent legislation indicates a trend to reduce such exemptions.

As indicated, most pesticide control laws have been classified as either "registration" or "use and application" laws; however, within the last 2 or 3 years, some "registration" laws have been amended to include sections on "use and application" of pesticides.

In Florida and a number of other States, such amendments have been made which restrict the use of certain pesticides. These restricted use pesticide laws generally authorize the Commissioner of Agriculture, or some governmental body, to determine which pesticides should be restricted in their use and to establish procedures regulating their purchase and application. The persistent pesticides were some of the first to be restricted in their use (except for some highly toxic rodenticides). The statutes defined them as, for example, pesticides which persist in the environment beyond one year from date of application (Florida), or which have a half life of over 18 months (New Mexico), or which accumulate in plant or animal tissues and are not eliminated in a reasonable time (New York). More recent listings of restricted pesticides include newer compounds which are highly toxic to humans, including some for which there is no known antidote.

The most common method of control is to require any person desiring to use a pesticide on the restricted list, to obtain a permit from a state or county official knowledgeable in the subject. The permit specifies the pesticide to be used, the crop to be treated, etc. Such pesticides may be sold only by a dealer licensed by the state to deal in such chemicals, and who may sell only to a person presenting a valid permit.

Alaska's 1970 pesticide law is a single act which relates to"...transporting, testing, inspecting, packaging, labeling, handling...advertising...and use of pesticides."

State pesticide laws governing tolerances for pesticide residues in or on raw agricultural commodities generally follow Sec. 408 of the Federal Food, Drug, and Cosmetic Act (Miller Amendment).

It should be kept in mind that a large part of pesticide control is accomplished by regulations issued under authority of the appropriate law; e.g., the Michigan custom applicators law states, "...the director may promulgate rules to carry out the provisions of this act...," and under this authority very specific details are issued regulating the use and application of pesticides.

Ordinances

A few local governmental bodies and municipalities have adopted ordinances and regulations which, in part, control the use of pesticides. Perhaps the most common are those which prohibit or restrict the use of highly toxic rodenticides or other pesticides by pest control operators in homes, warehouses, and structures. Some of the earliest local legislation related to fumigation practices in residences, ships, warehouses, etc.

The considerable amount of state and Federal legislation regulating pesticides has reduced the need for local ordinances; however, in the 15 states without use and application laws and in the two states without registration laws, local ordinances would be necessary if control of pesticides is to be accomplished.

REFERENCES

1/ 35 F.R. 15623

2/ Act of August 1, 1958, 72 Stat. 479, 16 U.S.C. 742d-1

3/ E.P.A. Organization and Functions Order No. 1110.2, 12-4-70

4/ 61 Stat. 163; 7 U.S.C. 135 et. seq.

5/ 36 Stat. 335

6/ 73 Stat. 286

7/ 7 C.F.R. 362.2(c)

8/ P.L. 88-305, May 12, 1964 ["...all existing registrations (issued) under protest shall terminate..."]

9/ 52 Stat. 1040; 21 U.S.C. 301 et.seq.

10/ This Act replaced the Food and Drug Act of 1906; U.S.C., 1934 ed., Title 21, Secs. 1-15; upheld; U.S. v. 74 Cases of Grape Juice, D.C. N. Y. 1910, 181 F 629.

11/ 68 Stat. 511; 21 U.S.C. 3462 (Miller Amendment)

12/ 62 Stat. 1155; 33 U.S.C. 466 et. seq.

13/ Reorganization Plan No. 2 of 1966.

14/ 30 Stat. 1152; 33 U.S.C.A. 407
The Rivers and Harbors Appropriation Act of 1899 represented a compilation and revision of existing laws relating to navigable waters. [Acts of 1886 (24 Stat. 329), 1888 (25 Stat. 209), 1890 (26 Stat. 453), 1894 (28 Stat. 363)]. The Act prohibits throwing, discharging or depositing any refuse matter of any kind or description, other than that flowing from streets or sewers in a liquid state, into any tributary of any navigable water. Also prohibited is the depositing of such material on the bank of navigable water so that it is liable to be washed into the water so as to obstruct navigation.

The law has been upheld on a number of occasions:

(1) U.S. v. Republic Steel Co. (1960) 5/4 decision.
[362 US 482, 4 L.Ed.2d 903]
[rehearing denied, 363 U.S. 858, 4 L.Ed.2d 1739]
The phrase "refuse flowing from sewers in liquid state" means "sewage."
Industrial deposits create an "obstruction."
Matter in suspension in water discharged into navigable river is not saved by the (exception clause) in the act.

(2) U. S. v. Standard Oil Co. (1966) 6/3 decision reversed lower court.
Commercially valuable gasoline discharged into a navigable river when shut-off valve was accidentally left open was within (Act) ban on depositing any "refuse matter" of any kind or description in navigable waters. The word "refuse" does not demand that the material must have been deliberately thrown away; it is satisfied by anything that has become waste, however useful it may earlier have been.

15/ E. O. 11574, Dec. 23, 1970 (35 F.R. 19627)

16/ Department of Transportation established April 1, 1967
49 USCA 1652; P.L. 89-670.

17/ 14 C. F. R. 137

18/ 16 C. F. R. 416; 35 F.R. 12727

METHODS FOR SAMPLING CHEMICALS IN THE ENVIRONMENT

Bill L. Stevenson

To promptly and accurately evaluate chemical pesticides in biological and environmental media, suitable representative samples of these systems insure quality analytical performance.

The identification and evaluation of pesticides present in samples submitted to a laboratory may serve as a basis for the documentation of an accident or incidental contamination from normal use. Laboratory data is a necessity to identify current and potential public health problems and protect the environment from unanticipated contamination.

Data from a competent laboratory based upon improper sampling can lead to false conclusions concerning the pesticide profile of the sample even though properly analyzed. For example, let us assume that a laboratory making routine blood analysis of the general population in a given area is consistently, but erroneously, finding higher pesticide levels than is being reported by similar laboratories in other areas. Plotted on a national scale, it would then appear that the people of this area are being exposed to higher levels of pesticides than the rest of the national population.

Another example can be cited which involved complaints filed by several women employees making draperies for mobile homes that some irritant was present in the atmosphere. An investigation was made and a survey of the work area revealed that the entire operation, including the storage of bolts of drapery cloth, was confined to a room 12' x 15' with a 3/4 ton air conditioner providing the only ventilation.

Through a literature review, it was learned that formaldehyde is used to make colors "fast" in the dyeing process of cloth. This information indicated a possible source of the problem.

The sampling procedure followed (to determine exposure levels to atmospheric formaldehyde in work areas) was recommended by an excellent and authoritative source. However, one small but important detail was omitted in the sampling instructions--that was to use an impinger with a diffusion attachment to disperse the air stream into tiny bubbles for greater absorption in the collection media. This omission resulted in a [illegible]lse reading indicating a safe working environment when in fact, the formaldehyde vapors exceeded established threshold limits. A law suit was instituted and was an embarrassment to all concerned.

Interferences are encountered in most analytical methods; therefore, it is rare that a method is free from all interferences regardless of the concentration of chemicals in a sample. Nevertheless, most methods will yield reliable results with little interference when followed as presented by authoritative and approved methods.

Analytical procedures are usually designed either to give the total amount of an element present in a sample or to give the amount of a certain definite solute species. Interferences affect either type of analytical procedure and the results are a serious potential source of error against which the analyst must always be aware.

The following general rules for sampling can be utilized in most investigations:[1]

1. Never take a composite sample unless the subject area to be sampled is known to be uniformly contaminated.

2. Take a number of samples from the subject area that would best represent possible areas of contamination.

3. Take the samples immediately, when reason for concern is apparent. It may be too late - later.

4. Label the samples with all the information immediately. You may forget later.

5. Preserve the samples with whatever means are necessary. This may be refrigeration, freezing, formaldehyde or solvent.

6. Make sure the means of preservation is compatible with subsequent analysis. Samples of crab eater seals and penquins from the Antarctic were shipped back to this country wrapped in plastic. As a result the reported levels of DDT are questionable due to the plasticizer in the plastic. Don't preserve samples to be used for chlorinated hydrocarbon analysis with chloroform. Don't preserve samples for phosphate analysis with formaldehyde. If you don't know what analysis will be required, refrigeration is your best bet.

7. Take a large enough sample. Tomorrow will be too late to get more.

8. Be prepared to take samples. Have sampling tools needed, knives, scissors, trowels, spoons, etc. Have suitable bottles for samples.

9. Label all samples.

10. Write a description of the situation as the investigator sees it at time of sampling. It is not unusual for the cost of analysis in particular investigations to run $10,000. This expenditure should

not be jeopardized because the sampler is too lazy to write down the situation as he sees it. Provide a case history. This is needed for the chemist to get a clue as to what to analyze for. He cannot possibly screen for the million or so compounds that presently contaminate our environment.

11. Get samples to laboratory now. Don't wait two weeks while you talk the situation over.

Procedures for taking samples:

Although pathologists should have adequate knowledge concerning the collection and submission of autopsy samples for chemical analysis, occasionally samples are contaminated by using improper containers or solutions that interfere with analytical methods.

Samples from suspected human poisonings:

1. Quantity:

   a. Tissue - 1-5 grams
   b. Vomitus - 2 ounces or more
   c. Stomach content - 2 ounces or more
   d. Stomach wall tissue - 5 grams or more
   e. Kidney - 1-5 grams
   f. Liver - 1-5 grams
   g. Blood - 5-10 ml
   h. Urine - 5-10 ml
   i. Brain - 1-5 grams

2. Packaging: Each tissue sample should be isolated in a separate chemically clean glass jar or bottle.

3. Shipment: It is preferable to have the samples frozen and shipped on Monday to the appropriate laboratory. When samples are frozen, care should be taken that enough dry ice is included to insure arrival of samples in a frozen condition.

Soils: The area should be searched carefully for oil spots or areas that look different from the surroundings. These can be sampled by using a sampling tool made from a tin can or similar container. Cut both top and bottom out evenly. Wash well and repeatedly. Rinse in clear water. Press this can in suspect area to depth of 1-1/2 - 2 inches and remove from soil. Punch core taken into new quart mason jar. Take several more cores from same areas. Seal jar and send to the laboratory after careful marking to indicate where sample was taken, when, by whom, and number and depth of cores.

Water: Water samples should be submitted in chemically clean one-gallon glass bottles.

Most natural water bodies are not completely homogeneous, and obtaining a truly representative sample will depend on the sampling technique employed, as well as the size and number of samples collected.[2] Proper sampling of large bodies of water should include a surface sample, an intermediate sample and a bottom sample. Always use chemically clean glass bottles for collecting samples.

Interfering elements are leached from plastic; therefore, plastic sample bottles should never be used to collect samples for pesticide analysis.

Swab Samples: Sampling to determine contamination on a wall or duct or other surfaces may be collected through the use of sterile wool, some medical alcohol or acetone and plastic throw away gloves. Wearing the gloves, wash the suspect area with swabs of cotton and solvent using care not to let solvent squeeze out of the swab. Place used swab in pint mason jar. Repeat on adjacent area. When labeling bottle,record where sample was taken, by whom, how it was sampled and how large an area.[1]

The following tables provide information for proper sample collection; i.e., size of sample, packing storage, preservatives and other helpful information.[1]

BIBLIOGRAPHY

1. Barthel, W. F., Sampling Procedures for Chemicals in the Environment, Atlanta Toxicology Branch, Division of Pesticide Community Studies, Environmental Protection Agency, Chamblee, Georgia.

2. Brown, Eugene; Skougstad, M. W. and Fishman, M. J., Methods for Collection and Analysis of Water Samples for Dissolved Minerals and Gases.

Table 1

AIR SAMPLING

Sampling of air requires sophisticated equipment and methods. Consult State Services Section for information.

OTHER SAMPLING

Many other types of sampling are occasionally required such as grain, feed, flour, food or other types of samples representing human or animal exposure. It is highly important in such cases to inspect carefully the material to be sampled in order to detect possible areas of contamination. Sometimes only one sack in a shipment will show an oily spot of contamination, or the colored grain denoting seed treatment. Samples should be drawn both from suspect and non-suspect areas and so labeled. If in doubt, call the appropriate laboratory for guidance.

LABELING AND SHIPPING

Without proper labeling or shipping, all the care and trouble of taking the samples is wasted. Be sure the label is explanatory and well attached. Ship samples on a Monday so that they arrive during the week and not over the weekend where they might sit in a hot airport terminal and deteriorate. If the samples are worth taking, they are worth packing well and with a little extra dry ice or other refrigerant.

Attachment A

Type	Poison Examples	Types of Samples Needed
Chlorinated hydrocarbons	Aldrin Dieldrin DDT Endrin, etc.	Stomach and its content, vomitus, kidney, liver and fat.
Fluorinated compounds	1080 Sodium fluoride	Stomach and its content, or vomitus if present, liver, kidney and heart.
Inorganic phosphides	Zinc phosphide	Stomach and its content, vomitus, liver and spleen.
Organic phosphates	TEPP Parathion, etc.	Stomach and its content, vomitus, brain, heart, blood (if not deteriorated).
Phosphorous	Elemental phosphorous	Stomach and its content, vomitus, liver and kidney.
Cyanide	Cyanogen Sodium cyanide	Stomach and its content, vomitus, throat tissue, heart, brain and lung tissue.
Alkaloids	Strychnine	Stomach and its content, vomitus, liver and kidney.
Thallium	Thallium sulfate	Stomach and its content, vomitus, liver, kidney, leg muscle and bone.
Cardiac glucosides	Red squill	Stomach and its content, vomitus and a portion of intestine.
Lead	Lead acetate Lead arsenate	Stomach and its content, vomitus, liver, kidney, and long skeletal bones (leg).
Anticoagulants	Warfarin Pival PMP Diphacin	Stomach and its content, vomitus, heart, liver and blood.
Miscellaneous poisons, toxic compound unknown		Stomach and its content, vomitus, heart, liver, kidney, brain, blood and bone.

[illegible]ABL[illegible] E[illegible]ron[illegible]al [illegible]pling

SAMPLE	SIZE OF SAMPLE	PACKING*	STORAGE	PRESERVATIVE	OTHER INFORMATION
SAMPLING OF WATER FOLLOWING INCIDENT					
private well	1 gallon	glass	ambient	none	description of well date
municipal pre filter at filter treated	1 gallon ea.	glass	ambient	none	note where and when taken
river	1 gallon	glass	ambient	none	detailed location of sampling site and date
lake	1 gallon	glass	ambient	none	detailed location of sampling site and date

Accompanying each set of samples should be a complete description of incident and all pertinent information to guide laboratory director in making analysis.

SAMPLE	SIZE OF SAMPLE	PACKING*	STORAGE	PRESERVATIVE	OTHER INFORMATION
SAMPLING OF TISSUE AT AUTOPSY					
fat	1 to 5 gms	glass bottle or aluminum foil	frozen or 10% Formaldehyde		name of subject site of sample sample size date, cause of death
liver lung brain gonads spleen muscle, etc.	1 to 5 gms	glass bottle or aluminum foil	frozen	not acceptable	name of subject name of tissue sample size date, cause of death

* Where glass containers are specified they should be fitted with teflon or aluminum lining.

TABLE I Environmental Sampling (Cont.)

SAMPLE	SIZE OF SAMPLE	PACKING	STORAGE	PRESERVATIVE	OTHER INFORMATION
		SAMPLING OF BODY FLUIDS			
urine for chlorinated hydrocarbons	**25 ml of 24 hr. sample if possible	glass	ambient	1/10% Formaldehyde	name of subject description whether 24 hr. or not
urine for phosphates	**25 ml of 24 hr. sample if possible	glass	frozen	none	name of subject description, whether 24 hr. or not.
blood for chlorinated hydrocarbon	1-5 ml plasma	glass tube oxaloted	frozen	none	name of subject reason for analysis date, physician
blood for phosphates	1-5 ml whole blood	glass tube oxaloted	frozen	none	name of subject reason for analysis date, physician
blood for cholinesterase	1-5 ml plasma	glass tube heparinized	refrigerated	none	name of subject reason for analysis date, physician
	1-5 ml red cells	glass tube heparinized	refrigerated	none	name of subject reason for analysis date, physician

** A complete case history should be provided with all human samples.

TABLE I Environmental Sampling (Cont.)

SAMPLE	SIZE OF SAMPLE	PACKING	STORAGE	PRESERVATIVE	OTHER INFORMATION
		OTHER SAMPLING			
soil	1 lb.	glass or metal can	ambient	none	description of site, amount sampled, by whom and why.
sediment	1 lb.	glass or metal can	ambient	none	description of site, amount sampled, by whom and why.
wildlife birds mammals or reptiles	20 gms muscle (20 gms fat if possible)	glass	frozen	none	detailed description of sampling site name of animal approx. age if known by whom and why.
fish	20 gms tissue	glass	frozen	none	detailed description of sampling site name of animal approx. age if known by whom and why.

Analysis of one animal, fish or bird will generally tell but little. Enough animals should be sampled to provide a crossection exposure picture of the incident but certainly never less than 10 subjects.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL COMMUNICABLE DISEASE CENTER
PESTICIDES PROGRAM
ATLANTA, GEORGIA 30333

FORM APPROVED
BUDGET BUREAU NO. 68-R

1. D100987

COMMUNITY STUDIES PROJECT ON PESTICIDES
ACUTE EXPOSURE RECORD

PARTICIPANT'S NAME

2. PROJECT CODE # ___ ___ 3. GROUP ID ___

4. AMA ID # ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

PARTICIPANT'S ADDRESS *(include zip code)*

EMPLOYER'S ADDRESS *(include zip code)*

6. *(D050)* 1 ☐ URBAN 2 ☐ RURAL 3 ☐ UNKNOWN

DATE OF BIRTH	PHONE	SEX	RACE
___/___/___			

5. INTERVIEW DATE ___/___/___

7. MARITAL STATUS:

1 ☐ Married 2 ☐ Widowed 3 ☐ Divorced 4 ☐ Single

INTERVIEWER'S NAME

EMPLOYER

8. SOURCE OF DATA: 1 ☐ Participant 2 ☐ Employer 3 ☐ Relative
4 ☐ Other *(If other than participant, give name)* ____________

9. CURRENT OCCUPATION: *(D010)*

CODE (INDEX I) ___

NUMBER OF YEARS ___ *(Report to nearest year)*

10. CHIEF COMPLAINT: *(D020)*

(Mark (x) by any symptoms which occurred as part of the chief complaint.)

CODE

00 ☐ none
01 ☐ malaise
02 ☐ fatigue
03 ☐ confusion
04 ☐ headache
05 ☐ nervousness
06 ☐ hyperirritability
07 ☐ light-headedness
08 ☐ fainting
09 ☐ dizziness
10 ☐ dermatitis
11 ☐ coma, unconsciousness
12 ☐ skin flushing
13 ☐ increased sweating
14 ☐ cyanosis
15 ☐ blurred vision
16 ☐ increased tearing
17 ☐ rhinitis
18 ☐ nasal stuffiness
19 ☐ increased salivation
20 ☐ tightness in chest
21 ☐ difficult breathing
22 ☐ palpitations
23 ☐ nausea
24 ☐ vomiting
25 ☐ abdominal pain, cramps
26 ☐ diarrhea
27 ☐ muscular weakness
28 ☐ tremor, fasciculations
29 ☐ convulsions
30 ☐ paresthesiae
31 ☐ other (specify) ____________
32 ☐ fever

PRESENT ILLNESS

11. CASE TYPE: *(D030)* *(Mark (x) in block by appropriate answer)*

1 ☐ Accidental-home
2 ☐ Nonaccidental-occupational
3 ☐ Accidental-occupational
4 ☐ Suicide or attempted suicide
5 ☐ Homicide
6 ☐ Other ____________

12. DATE AND PERIOD OF EXPOSURE: *(D040)*

began (date) ___/___/___ (time) ___ ___ ___ ___
ended (date) ___/___/___ (time) ___ ___ ___ ___
(Use 24 hour clock)

13. SUSPECTED AGENT(S): *(list chemical names of pesticides and solvents. If only brand name is available, record and look up chemical name later.)*

NAME	FORM (E.G. DUST, LIQUID, ETC.)	CODE (INDEX II)	APPROX. AMOUNT (IF INGESTED)
	(D050)	___/___/_____	mgm
		___/___/_____	m
		___/___/_____	mg
		___/___/_____	mgm
		___/___/_____	m
		___/___/_____	m
		___/___/_____	mgm

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14. PROBABLE MAIN ROUTE OF EXPOSURE: *(D060) (Mark (x) in block by appropriate answer)*

1 ☐ oral 2 ☐ dermal 3 ☐ inhalation 4 ☐ combination or other

15. PHRASE WHICH BEST DESCRIBES SOURCE OF AGENT: *(D070) (Mark x) in block by appropriate answer)*

1 ☐ unknown or not applicable
2 ☐ bought in store
3 ☐ bought from door-to-door salesman
4 ☐ chemical taken from work
5 ☐ chemical taken from elsewhere
6 ☐ applied by commercial firm
7 ☐ applied by other person
8 ☐ provided by employer for job
9 ☐ other ______________________

6. WHICH BEST DESCRIBES CONTAINER? *(D080) (Mark (x) by one item from each column)*

A

1 ☐ original container, labeled
2 ☐ original container, unlabeled
3 ☐ other container, unlabeled
4 ☐ other container, mislabeled
5 ☐ other (specify ______________________)

B

6 ☐ paper sack or bag
7 ☐ plastic sack or bag
8 ☐ bottle
9 ☐ can or drum
10 ☐ other (specify ______________________)

17. WHICH BEST DESCRIBES STORAGE AREA AT HOME OR AT PLACE WHERE POISONING OCCURRED? *(D090)* Mark (x) in one box in each column. *(USE ONLY IF QUESTION 11 ABOVE INDICATES HOME CASE TYPE)*

A

1 ☐ locked
2 ☐ unlocked

B

3 ☐ kitchen
4 ☐ bathroom
5 ☐ closet
6 ☐ garage, shed, etc.
7 ☐ other (specify ______________________)

C

8 ☐ below ground or floor level
9 ☐ 1–4 feet above ground or floor level
10 ☐ 4–8 feet above ground or floor level
11 ☐ 8+ feet above ground or floor level

18. WHICH CIRCUMSTANCES CONTRIBUTE TO PESTICIDE INTOXICATION IN THE OCCUPATIONALLY-EXPOSED? *(D100)* Mark (x) for items which best describes. *(USE ONLY IF QUESTION 11 ABOVE INDICATES OCCUPATIONAL CASE TYPE)*

1 ☐ unknown
2 ☐ spillage
3 ☐ equipment malfunction
4 ☐ poor ventilation of work environment
5 ☐ poor application techniques, or poor work practices
6 ☐ drift
7 ☐ too early re-entry after fumigation
8 ☐ intentional (specify ______________________)
9 ☐ other (specify ______________________)

9. WHICH CIRCUMSTANCES CONTRIBUTE TO PESTICIDE INTOXICATION? *(D110)* Mark (x) for items which best describe *(THIS IS TO BE FILLED OUT IN EVERY INSTANCE)*

1 ☐ unknown
2 ☐ ate or drank from container
3 ☐ ate bait
4 ☐ ate contaminated soil
5 ☐ drank contaminated water
6 ☐ other oral source (specify ______________________)
7 ☐ handled container or pesticide
8 ☐ handled contaminated object (e.g. glove) (specify ______________________)
9 ☐ exposed to contaminated soil or water
10 ☐ other dermal source (specify ______________________)
11 ☐ inhalation when foam or sponge rubber furniture was present
12 ☐ inhalation when change in ambient temperature was causally related (specify ______________________)
13 ☐ other inhalation (specify ______________________)

0. DID THIS PATIENT TAKE ANY OF THE FOLLOWING DURING THE LAST WEEK? *(D120)* 1 ☐ Yes 2 ☐ No 3 ☐ Unknown
(if yes, mark (x) in box by appropriate items below, and provide requested information)

	NAME	QUANTITY/UNITS/ FREQUENCY (HRS.)	DATE AND TIME LAST TAKEN	
			MO/DA	TIME (use 24 hour clock)
alcohol		(D121)	___/___	____
sedatives		(D122)	___/___	____
rcotics		(D123)	___/___	____
henothiazine tranq.		(D124)	___/___	____
carbamate tranq.		(D125)	___/___	____
		(D126)	___/___	____
		(D127)	___/___	____

21. HOW LONG HAD PESTICIDES BEEN AVAILABLE AT EXPOSURE SCENE? *(D130)*

1 ☐ not applicable or unknown
2 ☐ hours
3 ☐ days
4 ☐ weeks
5 ☐ months
6 ☐ years

238 PROTECTIVE MEASURES IN USE DURING THIS EXPOSURE: (D140) (mark (x) in block by approp.answer

1 ☐ none
2 ☐ rubber gloves
3 ☐ mask or respirator
type ____________

4 ☐ rubber boots
5 ☐ long sleeves
6 ☐ coveralls
7 ☐ apron

8 ☐ rubber suit
9 ☐ goggles
10 ☐ other (specify ____________

23. WHICH OF THE FOLLOWING FIRST-AID MEASURES WERE INSTITUTED IMMEDIATELY? *(D130)*

1 ☐ none
2 ☐ change clothes
3 ☐ wash exposed area with soap and water
4 ☐ wash exposed area with other solvent

5 ☐ bath or shower
6 ☐ vomiting induced *(method* ____________
7 ☐ gave antidote *(specify* ____________

24. HOW MANY HOURS ELAPSED BETWEEN EXPOSURE AND BEGINNING OF COMPLAINTS?

(D160) — — hrs. *(D161)* — — min.

25. HOW MANY HOURS HAD COMPLAINTS BEEN APPARENT BEFORE MEDICAL ATTENTION RECEIVED?

(D170) — — hrs. *(D171)* — — min

26. WHAT COMPLAINTS (SYMPTOMS) OTHER THAN THOSE IN THE CHIEF COMPLAINT WERE ASSOCIATED WITH THIS ILLNESS? *(D180)*

00 ☐ none
01 ☐ malaise
02 ☐ fatigue
03 ☐ confusion
04 ☐ headache
05 ☐ nervousness
06 ☐ hyperirritability
07 ☐ light-headedness
08 ☐ fainting
09 ☐ dizziness
10 ☐ dermatitis

11 ☐ coma, unconsciousness
12 ☐ skin flushing
13 ☐ increased sweating
14 ☐ cyanosis
15 ☐ blurred vision
16 ☐ increased tearing
17 ☐ rhinitis
18 ☐ nasal stuffiness
19 ☐ increased salivation
20 ☐ tightness in chest
21 ☐ difficult breathing

22 ☐ palpitations
23 ☐ nausea
24 ☐ vomiting
25 ☐ abdominal pain, cramps
26 ☐ diarrhea
27 ☐ muscular weakness
28 ☐ tremor, fasciculations
29 ☐ convulsions
30 ☐ paresthesiae
31 ☐ other (specify ____________
32 ☐ fever

TREATMENT AND CLINICAL COURSE *(present illness)*

27. NAME OF ATTENDING PHYSICIAN

____________ MD

PHYSICIAN'S ADDRESS *(include zip code)*

29. NAME OF HOSPITAL

____________ No. days hospitalized *(D190)* — — —

30. TREATMENT

Treatment is presumed to include the usual supportive measures such as airway, oxygen, necessary IV fluids, etc. Hence these need not be mentioned unless their omission has contributed to the course. The medicine should include all pertinent ones, but single doses of aspirin, etc., may be omitted.

The physician need not detail each single dose as an individual listing. Rather, each change in schedule should be noted. The response should be either clinical or pharmacological and should be descriptive rather than a value judgment, for example:

EXAMPLE:

MEDICINE	CODE (INDEX III)	DOSAGE	TOTAL AMOUNT	RESPONSE
Atropine	1 4	0.8 mgm IV q min x 8	6.4 mgm	pulse, dilated pupils
Atropine	1 4	0.8 mgm IV q 1 hr x r	3.2 mgm	recovered consciousness
2-PAM	4 1	1 gm IV slowly	1000.0 mgm	no clinical;

MEDICINE	CODE (INDEX III)	DOSAGE	TOTAL AMOUNT	RESPONSE
(D200)	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	

31. OUTCOME:

(D210) 1 ☐ fatal   2 ☐ recovered   3 ☐ residual damage

. FINAL DIAGNOSIS:

(D220) 1 ☐ pesticide intoxication   2 ☐ solvent intoxication   3 ☐ drug intoxication   4 ☐ other

. CONFIRMATION OF ETIOLOGIC AGENT:

XAMPLE

AGENT	CODE (INDEX II)	SOURCE	CODE	CONCENTRATION	UNITS	METHOD
Parathion	8/04/_290	Container	6	5000	ppm	EC
Parathion	8/04/_290	Vomitus	1	500	ppm	U/V
PNP	0/07/_478	Serum	2	2	ppm	Elliott
PNP	0/07/_478	Urine	3	45	ppm	Elliott

AGENT	CODE (INDEX II)	SOURCE	CODE	CONCENTRATION	UNITS	METHOD
(D230)	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	
	_/__/____		_		ppm	

4. HAS SUBJECT HAD A PREVIOUS EPISODE OF PESTICIDE POISONING? *(D240)* 1 ☐ yes   2 ☐ no   3 ☐ unknown
(if yes, give date, etc., below)

Dates (mo./yr.)	Has PHS 1.165-4, ACUTE EXPOSURE RECORD, been completed for each episode? Yes	No
(D241) __/__	1 ☐	2 ☐
__/__	1 ☐	2 ☐
__/__	1 ☐	2 ☐
__/__	1 ☐	2 ☐

*If PHS 1.165-4 has not been completed complete one now.

5. WERE OTHER WORKERS OR FAMILY MEMBERS ALSO EXPOSED OR ILL? *(D250)* 1 ☐ Yes   2 ☐ No
How many? __ *(Give details below)*

. CONCLUDING REMARKS: *(D260)* 1 ☐

PESTICIDES IN AN OCCUPATIONAL SETTING (PESTICIDE INDUSTRY)

Louis Kaplan

The New Jersey Pesticide Project has a certain advantage over the other State Projects in the Pesticide Community Studies Program in that we have a large concentration of pesticide plants. Because we do have so many plants, much of the information and data for this report comes from our experience and work in New Jersey. It should be noted that there is really very little difference between a plant in New Jersey and one in Colorado or Florida, or any other state. I would like to make the point now that this is not a provincial or sectarian report, and that the observations and conclusions herein included apply equally, I am sure, to the workers in any other pesticide plant.

Our state has approximately 140 pesticide formulating, manufacturing and distributing plants, employing about 5000 pesticide-exposed workers. Most of the material in this presentation is derived from continuing studies of 132 pesticide workers in nine plants, and a one-shot concentrated study of a herbicide plant of 73 employees. Thus a total of 205 pesticide workers is involved.

Long-term participants in the program are given regular physical examinations, electrocardiograms, chest X-rays and a complete spectrum of biochemical examinations. Results are compared with a control group of 52 minimally exposed subjects. In addition, our field men are routinely in contact with the participants to keep their occupational and medical histories current.

Some general characteristics of most pesticide plants are: few employees (usually 20 or less), makeshift equipment and plant, minimal supervision, poorly designed exhaust ventilation, and insufficient and rarely used personal protective equipment and sanitation facilities.

Some, not all, plants of large national concerns present a different picture. Usually they employ more than 20 workers, are well supervised, supply uniforms and good personal protective equipment, occupy well designed quarters, and have

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adequate equipment for manufacturing, processing, ventilation, and prevention of environmental contamination problems.

Pesticide Plants in the Program

Perhaps a profile of a typical pesticide formulating plant would be helpful at this time.

Plant A - Profile of a Typical Pesticide Formulating Plant

Formulating Plant "A," located near Trenton, is engaged in the custom formulation of pesticide chemicals. Customers include many other New Jersey pesticide companies, Central Jersey farmers, custom pesticide applicators and pest control operators. This plant formulates a variety of pesticide chemicals, the fulk of which is organic phosphates and chlorinated hydrocarbons. A partial list of finished products includes: Parathion, Guthion, Malathion, Abate, Baytex, DDT, Aldrin, Chlordane, Lindane, Dieldrin and Sevin. This plant employs a total of 22; 19 male workers being directly engaged in pesticide handling activities. Employment is quite stable, with low turnover. Specific operations include milling and mixing of wettable powders and dusts, granule impregnation, liquid mixing, packaging, warehousing and shipping. Operations are to a large extent manual. There are small batch operations and larger production runs of single pesticides, such as Malathion.

The following protective equipment is supplied but its use is more or less left to the discretion of the individual: approved respirators, nuisance dust respirators, rubber gloves, rubber aprons, face shields and some hats. Fairly effective local exhaust ventilation is provided at the dust mill (feed site and discharge site of mixed pesticide dust) and the granular mill (bagging site). Design of hoods of these exhaust systems is poor and airborne contaminants can be observed in the plant environment. No local exhaust ventilation is provided for the liquid mixing operation, which is in the same building with the above-mentioned milling operations, located near a pyrethrin-blending operation in an adjacent building. Most workers spend the majority of their time within the main building and are exposed to pesticides, both at their particular duty station and contamination from adjacent operations. Plant housekeeping is a continuing problem, as the building is not particularly designed to facilitate clean-up. The bulk contamination of floors is usually removed by manual sweeping methods on a daily basis, usually toward the end of a work shift, which results in further contamination and exposure hazard. From time to time, when working with chlorinated hydrocarbons, the mixing operator has been observed preparing laboratory control samples with his bare hands. A number of acute pesticide intoxications have occurred here.

A few brief comments on some of the other plants are in order. One large plant provides dust milling by air-impaction methods, blending and packaging services. Although it formulates a number of compounds, the main pesticide formulated there is Carbaryl. This plant produced considerable amounts of DDT up until 1963, and serum residues of DDT and DDE are consistently high in those senior employees who formerly worked on DDT.

Another plant is a general formulating plant with intensive operations in liquid, granular and dust formulating of organophosphates. A lot of parathion work is done here. Although this is what we would call a "clean" plant, the employees are sufficiently exposed to the more toxic organophosphates to cause frequent cholinesterase depressions and complaints of dizziness, nausea, weakness, etc.

Other plants monitored are general formulating plants, where the workers are exposed to a variety of pesticides.

Some Results From the New Jersey Study (1970)

Appreciable differences in blood cholinesterase serum pesticide residues, urinary metabolites and biological testing continue to be observed in our pesticide exposed group, as compared to the controls. Periodic highly elevated DDT and DDE blood residues are being found in ex-DDT formulators. The highest value of 700 parts per billion was found in a service worker who has not formulated since 1958.

We continue to see a number of sub-clinical and clinical pesticide poisoning cases among our subjects, especially when exposed to the more toxic organophosphates such as parathion and phosdrin. In these plants, where toxic organophosphates are formulated, abnormal cholinesterase values were and are commonplace.

Twenty-six out of 85 cases of pesticide poisoning cases investigated by the Project are pesticide workers. Table 1 demonstrates percent abnormals in cholinesterase and pesticide residues.

TABLE 1

Abnormal Cholinesterase and Pesticide Residues in Industrial Workers

	Cholinesterase (I.U.)			Serum Residues (ppb)		
	No.	RBC (<8)	Plasma (<3)	DDT (>20)	DDE (>30)	Dieldrin (>5)
Industry	132	15%	24%	45%	61%	38%
Controls	64	8%	11%	0%	14%	0%

Table 1a compares serum pesticide residues of formulators, general population and controls.

TABLE 1a

Comparison - Serum Pesticide Residues (ppb)

	Controls		General Population		Formulators	
Residue	Mean	Range	Mean	Range	Mean	Range
p,p'-DDT	4.4	0-23	5.6	1-12	28.9	0-304
p,p'-DDE	14.3	0-27	20.8	7-67	28.0	2-187
Dieldrin	1.1	0- 6	1.3	0- 5	7.5	0- 64
Sample Size	54		57		65	

Table 2 reports the percentage of tests which were outside the normal ranges for the blood biochemistries. Some biochemical responses showing differences from the controls were: glucose, uric acid, cholesterol, calcium, lactic dehydrogenase alkaline phosphatase, transaminase (SGOT and SGPT), alkaline phosphokinase, creatinine, albumin.

TABLE 2

Biochemistry (SMA-12)

(Values cited are percentages of total tests showing abnormal results)

	Controls (N = 112)	Industry (N = 150)
Glucose	9.8	16.7
Uric Acid	3.6	7.3
Cholesterol	17.0	24.3
Calcium	3.6	9.4
LDH	16.1	24.7
Alkaline Phosphatase	8.1	17.7
SGOT	13.4	16.0
SGPT	4.5	8.0
CPK	6.2	9.3
Creatinine	0.9	5.4
Albumin	8.9	14.7

In a morbidity study, a review was made of all the positive and abnormal physical findings of our control group versus our pesticide industry group. These data were obtained by medical examinations and medical histories.

In Table 3 significant differences are noted in chronic cough and sinusitis, dizziness and headache, hearing difficulties and hypertension. Positive nervous system findings occur in 50 percent of the pesticide industry workers as compared to 35 percent of the controls. Gastrointestinal complaints were 7.5 percent in controls and 12 percent in industry. Back problems are twice as prevalent in the industry group.

TABLE 3

Number of Positive Physical Findings Pesticide Industry vs. Controls

Category	Controls (40)	Pesticide Industry (112)
Back Trouble	5	24
Chronic Cough & Sinusitis	6	31
Dizziness & Headache	3	18
Hearing	3	24
Hypertension	1	23
Nervous System	14	55
Gastrointestinal	3	13

Table 4 shows a comparison of environmental air samples taken in a plant which does a considerable amount of organochlorine formulating; as opposed to random outdoor sampling. Note the comparatively large amounts of DDT, DDE and DDD in the air of the pesticide plant. Also, please note that the plant residues are in mgm per cubic meter and the outside residues are in nanograms per cubic meter. Converting, we get 570,000 to 7,200,000 ng/M^3 of DDT in the plant, compared to 0.6-3.2 ng/M^3 in the outside ambient air.

TABLE 4

Comparison of Environmental Air Sampling*
(Range)

	p,p'-DDT	p,p'-DDE	p,p'-DDD
Plant A (mg/M^3)	0.57-7.2	0.018-0.20	0.027-0.43
Ambient Air (ng/M^3)	0.6 -3.2	0-1.0	0-TR

*In-plant sampling vs. random outdoor sampling.

Dr. George A. Reich, in analyzing data printouts of 1969 subset information generated by Mrs. Janet R. Daling from the State of Washington, found that in a group of 741 workers, 311 had a total of 411 reactions to pesticides. The greatest number of reactions resulted from exposure to the organophosphates. Ninety-three reactions were reported as a result of exposure to parathion. Symptoms reported, some of which are shown in Table 5, were: headache, nausea, dizziness, dermatitis, tearing, rhinitis, blurred vision, vomiting, fatigue, muscular weakness, difficult breathing, abdominal pain and a few others.[1]

TABLE 5

Major Symptoms Reported Due to Pesticides Among Workers

Chemical Class	Reactions*	Symptoms Occurring In 10% or More of Cases
Chlorinated Hydrocarbon Insecticides	68	Headache Nausea Dizziness Dermatitis
Chlorinated Hydrocarbon Herb, etc.	32	Dermatitis Rhinitis Tearing Headache
Organophosphates	243	Headache Nausea Blurred vision Dizziness

*Only chemical classes with at least 10 cases are included.

Studies from other plants throughout the country, such as in Florida, Colorado, Texas, California or South Carolina, confirms what has been found in New Jersey. Pesticide plants have the same exposure problems and the same working conditions wherever they may be.

Special Study in New Jersey Plant Producing Malathion

Cooperative arrangements were made with a large plant for Dr. Arthur E. DePalma, at the time Principal Investigator of the New Jersey Project, to examine past personnel and medical records of a group of employees who worked directly with organic phosphates, Malathion in particular, for a long period of time. This company has a medical department, where medical examinations and other pertinent testing are conducted on a regular basis. This plant is what we would term a "clean plant," in that housekeeping is excellent and protective equipment and protective measures are good. The workers examined were long-time employees, some going back 15 years or more. Production of Malathion started in 1951.

In an examination of the medical histories of 34 men, the following information was obtained:

Skin (20 incidents), and particularly eye irritations (237 incidents), were frequent but they seemed to lack chronic sequelae. Monthly cholinesterase testing was generally normal and occasionally, when abnormal, the particular individual was transferred out of organophosphate work. One case of systemic poisoning was found. Eighteen respiratory tract irritations were noted. Eight of the men revealed hypertension in more than one examination.

In summary, in this plant there were definite indications of a high incidence of skin and eye irritations, some respiratory tract irritations, some cases of hypertension, and one case of organophosphate poisoning. Aside from this, there were no other indications that these 34 men were suffering from any chronic adverse health effects.

Some Reports on Other Studies of Pesticide Workers

A study was made by Dr. A.P. Poland, et al of 73 employees in a 2,4,-D and 2,4,5-T plant. These compounds are organochlorine herbicides -- dichloro and trichloro phenoxyacetic acids.

Chloracne was found (mederate to severe lesions) in 18 percent of the workers. Sixty-six percent more had some degree of acne. No clinical porphyria could be currently found and one worker had persistent uroporphyrinuria. No systemic toxicity, differing from normal populations, was found.[2] We have just received information from a law firm that most of the former employees of this plant, which is now out of business, have filed Workmen's Compensation suits against the company.

A report was made by I. Hoogendam, et al, on a health survey of 300 workers in plants manufacturing aldrin, dieldrin and endrin (toxic organochlorine pesticides) over a period of up to nine years. Although no fatalities and apparently no permanent damage occurred, 17 of the workers had convulsive intoxications and five of the 17 had more than one convulsion.[3]

Nine cases of convulsions in pesticide workers handling Thiodan, a highly toxic chlorinated hydrocarbon insecticide, are reported in a paper by Dr. Thomas S. Ely, et al.[4]

Dr. I.R. Tabershaw, et al, made a follow-up study of 235 individuals three years after acute organophosphate poisoning. Of this group, 114 had clearly defined organophosphate poisoning. Forty-three of the 114 had complaints for more than six months after poisoning, and 33 still had complaints three years after intoxication. These complaints were in the following categories: optic, headaches, chest pains, shortness of breath, cardiovascular, neuropsychiatric and miscellaneous.[5]

Environmental, clinical and biochemical evaluations were made by Dr. M. Wasserman, et al over a five-year period on pesticide workers in a pesticide manufacturing plant in Israel. The report is based on data obtained by using the Cornell Medical Index questionnaire. One hundred and forty workers in the pesticide manufacturing plant were compared to 71 workers from a textile plant as the control group. The results indicated:

1. There was a high incidence of complaints in the pesticide workers group.
2. Both groups demonstrated similar frequency of complaints in those sections relating to mood and feeling patterns.
3. Higher incidence of positive answers in the pesticide group as far as the respiratory, cardiovascular and nervous systems are concerned.

4. In both groups, the number of complaints increased with age.

Table 6 lists positive answers to various sections of the CMI.[6]

TABLE 6

Positive Answers in CMI According to CMI Sections

Sections	Positive Answers (Mean) PMP*	Positive Answers (Mean) Control	Probability
Eyes & Ears	1.05	0.86	$p > 0.10$
Respiratory System	1.81	1.07	$p < 0.03$
Cardiovascular System	1.28	0.74	$p < 0.01$
Digestive System	3.27	2.48	$p < 0.05$
Musculoskeletal System	0.94	0.67	$p > 0.10$
Nervous System	1.77	1.15	$p < 0.03$
Genito-urinary System	0.92	0.76	$p > 0.10$
Fatigability	1.13	0.87	$p > 0.10$
Frequency of Illness	0.72	0.39	$p = 0.10$
Miscellaneous Diseases	1.11	0.77	$p < 0.10$

*PMP - Pesticide Manufacturing Plant

CONCLUSION

In summation, there is enough data on hand now to state that pesticide exposed workers in pesticide plants differ from minimally exposed controls in a number of parameters:

1. Abnormal cholinesterase (low) and abnormally high organochlorine residues in sera.

2. Blood Biochemistry - Higher rate of abnormals in glucose, uric acid, cholesterol, calcium, LDH, alkaline phosphatase, SGOT, SGPT, CPK, creatinine, and albumin.

3. Probable renal and hepatic dysfunctions, caused by excessive exposure to pesticides.

4. Morbidity, in the following categories: Back trouble, chronic cough and sinusitis, dizziness and headache, hearing, hypertension, nervous system, gastrointestinal, cerebrovascular, cardiovascular, nephritis and nephrosis, dermatitis.

5. Acute pesticide intoxications and sequelae - The number of acute cases of pesticide poisoning and the frequency of subacute cases far exceeds those reported in the general population.

Further research and investigations are necessary to confirm what has been found to date, and to relate the subtle effects of repeated pesticide insults on man's health to chronic disease states.

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CHANGING PESTICIDE PATTERNS

Dr. L. C. Gibbs

My assigned topic is somewhat like an octopus. There are so many [illegible] to it that you don't know where to grab hold and get started. Irrespective of my dilemma, I'll start off by saying that we've been experiencing changing pesticide patterns for years so changes as such don't really bother me. On the other hand, if we had looked at the rate of change, volume and kinds used, application techniques, effect on non-target organisms, persistency and other aspects, we would have been more concerned and some of the actions taken recently might have developed earlier.

Everyone pretty generally agrees that pest control is essential for protecting man, plants and animals from diseases, discomforts or annoyances and for insuring the production of an adequate supply of high quality food and fiber. The continuing need for pesticides has also been indicated in a number of studies. Included are the Ribicoff Committee (1964), two committees of the National Academy of Science-Pesticides in Foods and Feeds (1968) and Persistent Pesticides (1969), and the Mrak Commission (1969). These reports pointed out existing, as well as potential, problems which we are having to cope with today. Increasingly, emphasis in research, regulation, education and operating programs is being directed toward practicing and encouraging the use of the most effective means of pest control and/or management which will cause the least potential hazard to man, his animals, fish, wildlife and other components of the environment. In keeping with this policy, persistent pesticide uses have been and will continue to be reviewed use by use and only those uses considered essential and for which no substitutes are available will be retained. This means that many of the chemical uses producers have become accustomed to will be lost--some because there are safer less persistent substitutes and others because of their deleterious and cumulative effects on certain species of fish, wildlife, etc. and possible effects on man.

Today, pest control in the U.S. is practiced in the setting of a population growing in numbers, density, and affluence and with an intensified monocultural system of agriculture which is employing fewer and fewer people. Under this situation, we have perhaps placed too great a reliance on pesticides following the initial success of the new organic pesticides and the development of more efficient application techniques. The change in the pesticide patterns which have taken place over the years didn't just happen. They have been predicated and based on developments in research, technological advances, legislation, labor shortages, labor costs, economics, our system of agriculture, food standards, and other aspects related to an affluent society. To these, we must add another far-reaching consideration--concern for the environment. All points considered, we might say that our changing pesticide patterns, like other developments, are merely a reflection of the time and period in which we live.

In order to grasp the full significance of some of the developments that have taken place which have been instrumental in effecting changes in our pesticide use patterns, we need only to recall some of the major changes that have taken place in agriculture. Perhaps the first one we should note is that in the early history of agriculture, farming was diversified and our pest control knowledge and chemicals were limited to say the least. Even in the early 40's, we could still count our pest control materials on our fingers and the commonly available materials included items such as lime sulfur, Paris green, lead arsenate, nicotine sulfate, Rotenone and a few others. In contrast today, our pest control arsenal consists of over 250 basic chemicals available in some 45,000 registered products. Needless to say, almost everything has changed. Foremost among the factors which have been influencing changes in pesticide use patterns has been the shift toward development of an intensive monoculturistic system of agriculture. This system, for the sake of economy, has resulted in the concentration and culture of large blocks or acreages of a single or successions of the same crop. This alone has been conducive to a build-up of certain pests which required more pesticide use and in some cases resulted in the development of resistance to certain pesticides within some insect species. Increased production costs resulting from labor shortages, increased labor costs, etc. have also been conducive to mechanization and this in turn has fostered increased plant populations which further contributes to increased insect and disease problems. So you see, the circle goes round and round and never stops or stands still. Other factors include the passage of more stringent regulations and laws governing the registration, transportation, sale and use of pesticides, lowered residue tolerances, and the development of the carbamate and systemic type pesticides. One other factor which I have so far failed to mention specifically is the advances made in our analytical equipment and technology. Each factor or combination of factors in turn affects use patterns one way or another and the full impact or change can seldom be fully determined because of the complexity and interaction involved.

Any discussion of changing pesticide patterns would be remiss without some mention of use statistics and recent legislative and regulatory developments. First let's look at some aspects of use statistics since this is undoubtedly the area which has contributed most to some of our problems. Use, likewise has without question been the paramount factor responsible for the tightened legislative and regulatory actions which have been affected in the last few years. In looking at use statistics, I think that it is important that we look at the volume used and note the use trends developed within the three major classes of pesticides and within even a single class. The following tables, which are more or less self-explanatory, show what the use patterns and trends have been over the years for pesticides as a whole and for some within a group or class. See Table 1 for statistics on pesticide sales volume for fungicides, herbicides and insecticides. Table 2 is illustrative of trends and use patterns developed for the organochlorine type insecticides.

Table 1. Sales of organic pesticides by primary chemical manufacturers according to type of usage, 1962-1968

Type of Usage	1962		1963		1964		1965	
	Amount	% of Total	Amount	% of Total	Amount	% of Total	Amount	% of Total
(Volume of sales in 1,000 pounds)								
Fungicides	97,589	15.4	93,265	14.3	95,556	13.8	106,342	13.9
Herbicides	95,209	15.0	122,872	18.9	152,027	21.9	182,869	23.9
Insecticides	441,164	69.6	435,334	66.8	444,772	64.3	474,694	62.2
TOTAL	633,962		651,471		692,355		763,905	

Type of Usage	1966		1967		1968*		1969	
	Amount	% of Total	Amount	% of Total	Amount	% of Total	Amount	% of Total
(Volume of sales in 1,000 pounds)								
Fungicides	118,397	14.4	120,413	13.4	129,961	13.5	121,418	13.4
Herbicides	221,502	26.9	287,582	32.1	318,554	33.2	311,157	33.5
Insecticides	482,357	58.7	489,368	54.5	511,116	53.3	493,088	53.1
TOTAL	822,256		897,363		959,631		925,663	

*Preliminary Data

The use of persistent pesticides underwent more intensive discussion in 1969 than ever before. Although pesticides have contributed tremendously to preventing human disease and to increasing the production of food and fiber, mounting evidence indicated the need for concern about unintended effects on the environment, including injury to the health of man and livestock. Associated with the benefits from the use of pesticides are the risks of injury; and these risks are greater from the use of persistent chemicals. Restrictions have now been placed on the latter with special emphasis on DDT. Coupled with this have been numerous State legislative actions which relate to pesticide use, sale, record-keeping, applicator licensing, development of restricted use categories, etc. In this respect it is of interest to note that as of November 1970, 36 states had enacted pesticide applicator licensing laws. Other significant developments include complete restriction on the use of DDT in a number of states and the development of lists of chemicals limited to restrictive or permit uses.

U.S. production of pesticides continued to increase in 1968 to meet the rising consumer demand both at home and abroad. Production of synthetic organic pesticides increased 14 percent. The average annual growth was nearly 8 percent during the previous five-year period. Production of insecticides in 1968 increased 15 percent; herbicides, 17; and fungicides, 7.5. Available production data are limited mostly to synthetic organic pesticides. Statistics for them provide a good indication of growth, however, since they constitute an estimated 90 percent of U.S. pesticide production.

Evidence continues to accumulate showing that persistent ("residual," "long-lasting," "long-lived," or "hard") pesticides are contaminating the environment and adversely affecting various life forms within it. Persistent pesticides are those which dissipate or degrade slowly and whose residues remain in decreasing but measurable concentrations for varying periods of time, usually into the second growing season or longer. They are disseminated by natural forces and have characteristics that favor their accumulation and storage in living organisms.

The major persistent pesticides are commonly known as "organochlorine" compounds ("chlorinated hydrocarbons" or "polychlors"). They include aldrin, benzene hexachloride, chlordane, DDD, DDT, dieldrin, endrin, heptachlor, lindane, toxaphene, and certain others. Compounds containing arsenic, copper, lead, and mercury are also persistent.

In recent years, DDT has become a prime target of concern. Its usage began earlier and has been more widespread than that of other major persistent pesticides. For well over two decades, DDT has been the most generally effective and most widely used pesticide worldwide. It is best known for practically wiping out malaria in the United States and over large areas elsewhere. It has been a valuable tool in combating cholera, typhus, Rocky Mountain spotted fever, and encephalitis. Uninhabitable areas have been made more habitable and life has been made more comfortable for many people. DDT also has worked wonders for farmers. Its use has controlled many major insect pests, notably those troublesome to cotton, vegetables, and fruit.

Few food-producing areas are free of DDT contamination. There has been awareness of this for some years. The President's Science Advisory Committee in 1963 called attention to low-level contamination of the environment with DDT. As long as two decades ago, DDT residues in milk caused restriction to be placed on its use for controlling flies and other insects on dairy cattle.

Use of certain other organochlorines on forage grazed by dairy cattle was restricted for the same reason; namely, that residues appeared in milk.

Use of DDT in the United States during crop year 1968 was only 42 percent as much as in 1959. Its use peaked in 1959 at more than 78 million pounds but declined to less than 33 million by 1968.

Other organochlorine insecticides were developed following the introduction of DDT. The total usage of the more widely applied of these insecticides, including DDT, also peaked in 1959 at 156 million pounds but was down to 71 million in 1968 (Table 1). The 1968 level is only 46 percent of the 1959 usage, close to the 42 percent for DDT. Largely responsible for this decline are (1) increased insect resistance to insecticides, (2) the availability of less persistent insecticides which are efficient in insect control, and (3) the concern about the risks from use of persistent insecticides.

Much of the contamination from persistent pesticides may have resulted from excessive use. Although environmental contamination from past usage will continue for a period of years in lessening amounts, further reductions in usage and careful application of all pesticides can be expected to substantially lessen this type of pollution of the environment.

Table 2. Organochlorine insecticides: Producers' domestic disappearance of selected kinds by crop year, United States, 1955-1968

Crop year 1/	Aldrin-toxaphene 2/ group	DDT	BHC	Total
	1,000 pounds	1,000 pounds	1,000 pounds	1,000 pounds
1955	54,400	61,800	7,800	124,000
1956	61,570	75,000	9,450	146,020
1957	52,500	71,000	6,600	130,100
1958	78,834	66,700	5,500	151,034
1959	73,331	78,682	4,276	156,289
1960	75,766	70,146	5,111	151,023
1961	78,260	64,068	4,577	146,905
1962	82,125	67,245	2,404	151,774
1963	79,275	61,165	1,299	141,739
1964	83,161	50,542	3/	133,703 4/
1965	80,568	52,986	3/	133,554 4/
1966	86,646	46,672	3/	133,318 4/
1967	86,289	40,257	3/	126,546 4/
1968	38,710	32,753	3/	71,463 4/
1969	89,721	30,256	3/	129,977 5/

1/ Ends September 30.

2/ Includes aldrin, chlordane, dieldrin, endrin, heptachlor, Strobane and toxaphene.

3/ Not published separately to avoid disclosure, but probably less than in 1963.

4/ Includes only the aldrin-toxaphene group and DDT.

5/ Calendar year data.

Progress with Less Hazardous Controls. Research has already developed chemicals suitable for use to control many target pests and which are less persistent and more specific than the organochlorine insecticides. Readily degradable chemicals and biological, physical, and cultural controls as an integrated assault offer areas for research into possible answers to many uses of persistent pesticides. The emphasis on newer weapons includes the study and development of viruses causing insect diseases, sterilization of adult insects to disrupt their reproductive cycle, synthesis of natural insect attractive scents or effective substitutes as lures, ultraviolet light and ultrasonic sound as control agents, hormones that interfere with normal insect growth, and the manipulation of genes. Further research is being stimulated in the breeding and utilization of domestic and imported predatory and parasitic insects, long used as essential biological aids in the control of a number of insect pests.

Outstanding achievements include massive releases of sterilized male screwworm flies which have virtually wiped out this enemy of the southern and western cattle industry, and the application of milky disease spores which have infected and killed Japanese beetle grubs in the soil.

Selected examples of activities designed to control pests without using toxic chemicals or with reduced or limited amounts follow:

BIOLOGY AND CHEMISTRY

Control of Insect Diapause (resting state) by Light. Recent tests have determined the most effective wavelengths of light for breaking diapause of codling moth larvae and oak silkworm pupae. Diapause was prevented in some European corn borer larvae and imported cabbage worm pupae in an outdoor pilot test by extending day length. Similarly, diapause in pink bollworms was prevented in laboratory tests by short light periods at certain times during the dark cycle.

Effects of Light. Adverse effects of continuous light on the reproductive systems and mating behavior of the Indian-meal moth have been demonstrated. Light intensities of 200-foot candles or more inhibit or reduce egg laying by 25-50 percent of that occurring in the dark. Females inhibited by light normally retain their eggs until the day before their death and these eggs, laid under stress, show a very low percentage of hatch. Adults emerging from cultures reared in continuous light were slow to mate. Experimentation and morphological examination have shown that oviposition is triggered by the quantity of the spermatozoa in the spermathecae and not by the physical stimulus of the copulation. Further studies have shown that males reared under continuous light transfer very few spermatozoa to the females. The integration of these effects of the light regime offers considerable promise as a new method or as an adjunct to existing methods for controlling the Indian-meal moth.

Insect Hormones as Potential Control Agents. The natural ecdysones (molting hormones) and/or certain of their synthetic analogs cause termination of pupal diapause in a number of insect species. Studies on the mode of action and metabolism of radioactively labeled synthetic ecdysone analogs revealed that such compounds or their metabolites trigger the biosynthetic mechanism for the synthesis of the insect's own hormones. If metabolites of natural or synthetic ecdysone analogs that inhibit larval growth and reproduction can be found whose biological activity is greater than the parent compound, such chemicals might well serve as models for the preparation of safe and more potent agents for insect control.

Promising Biological Control Agents for Control of Aquatic Weeds. Studies of the *Marisa* snail in laboratory, greenhouse, and outdoor pools have shown considerable promise for its use in controlling submersed aquatic weeds in warm waters. More limited studies show the *Pomacea* snail to be even more effective in feeding on important aquatic weed species.

The white Amur fish which is indigenous to certain rivers in Siberia and northern China has given outstanding promise for control of aquatic weeds in experiments in European and some Asian countries. This fish is being used quite extensively in both temperate and subtropical areas of Asia for control of aquatic weeds and is an important food fish.

New Herbicide Formulation and a Combination Promise Greatly Increased Effectiveness and Safety in Control of Aquatic Weeds. A combination of 4 ppm of $CuSO_4$ and 1 ppm of diquat gives more positive and lasting control of hydrilla than 20 ppm of $CuSO_4$ or 3 ppm of diquat alone or than any of the many other herbicides and combinations that have been tested. The combination provides greater safety for fish, reduces the chemical cost considerably, and greatly reduces the chemical residues in water.

A new granular formulation of an amine salt of endothall provides control of hydrilla comparable to the much higher rates of liquid formulations previously used, confines the chemical residues mostly to the bottom two feet of a lake or pond, reduces the amount of herbicide required, and eliminates or greatly reduces the fish toxicity involved in use of liquid formulations.

Biochemical Factor in Corn Provides Resistance to European Corn Borer. A natural constituent of corn DIMBOA has been found responsible for resistance to the European corn borer and may help scientists breed superior resistance into hybrid lines. During the recent research, an accurate, objective method was developed for determining the DIMBOA in corn. This enables new lines of corn to be screened chemically for corn borer resistance. This is more rapid than the previous visual screening and its correlation with the visual screening of field plants was very high.

Uptake of a Systemic Fungicide by Elm Seedlings. Benomyl may be a promising fungicide for the control of Dutch elm disease. Benomyl was readily taken up by the seedling roots and by a newly developed technique, detected throughout the plant. The recent discovery and development of several systemic fungicides have given new impetus to the search for chemotherapeutic agents which will control the Dutch elm disease. This approach is especially significant since DDT up until recently has been the major chemical control for this pest.

Microbial Insecticide Lethal to Defoliators. Continuing studies of the pathogenicity and mode of action of Bacillus thuringiensis in forest insects have shown that the spores and crystals produced by the bacterium affect insects in different ways. The western hemlock looper is killed by the crystals alone; Douglas-fir tussock moth, western tent caterpillar, and the gypsy moth are most susceptible to the spores and crystals combined. Chemical constituents of host tree foliage affect pathogenicity, also.

A Highly Virulent Strain of Bacillus Thuringiensis, Designated as HD-1. Two commercial companies produced pilot plant quantities of HD-1 which were supplied to qualified research workers at several locations. Test results are extremely promising for control of cabbage looper and Heliothis spp. Progress is being made toward standardizing formulations in terms of International Units per milligram of the delta endotoxin.

Biological Control of Imported Cabbageworm. Imported cabbageworm (Pieris rapae) was effectively controlled by innoculative releases of the egg parasite, Trichogramma evanescens and the larval parasite, Apanteles rubecula, by maintaining the host population at a sufficiently high level to provide an adequate constant food resource for the parasite. This was accomplished by programmed releases of reared adult Pieris rapae.

Control of Lepidopterous Insect Populations with Inherited Sterility. Although moths are more resistant to radiation sterilization than other insects, they were found to be prone to pass on to their progeny radiation damage causing sterility in the next generation. In contrast to fully sterilized moths, which were noncompetitive, cabbage looper moths treated with three-sevenths of a sterilizing dose were able to compete with normal moths for mates. In laboratory and preliminary field cage tests, both male and female progeny of irradiated males were almost completely sterile, preventing a population increase in the second generation. Additional research is needed to determine if this technique can be used for practical control of insect pests, as a contribution to the development of new methods of control that will not adversely affect other organisms or pollute the environment.

Insect Attractants. New synthetic attractants much superior to those currently in use were discovered for European chafer, Japanese beetle, and yellow jackets. Four terpenoid compounds were isolated from male boll weevils which when properly combined attract both male and female weevils; the compounds were identified and synthesized. The synthetic material was highly promising in limited field tests. Commercial production of the attractant will provide material for use in an extensive field study to determine the feasibility of eradicating the boll weevil in an integrated program utilizing several methods to destroy the weevil.

Importation of Insect Parasites. Over 125,000 living specimens of 33 exotic or recently established parasites and predators were distributed for release in 29 states to aid in the control of 15 kinds of insect pests. Reports from cooperators during the year indicate new establishments of parasites that attack cereal leaf beetle, alfalfa weevil, elm bark beetle and greenbug in Michigan, Virginia, Ohio, and Oklahoma respectively.

Biological Control of Nematodes. Heavy application of chitin to field soil controlled root-knot nematodes on tomato; this was due to microbial activity of chitinoclastic actinomycetes. Control of root-knot lasted for two years. Several ammonium fertilizer salts controlled root-knot in pot test, but were inconsistent in field tests. Radio-labeled EDB and DBCP was taken up by nematodes and nematode-trapping fungi; there was no appreciable lethal effect on the fungi, indicating these nematicides will not destroy these beneficial soil fungi. Culture filtrates from Aspergillus niger were toxic to citrus and lesion nematodes. Chromatographic analysis of filtrate and subsequent tests indicate that oxalic acid was the toxic fraction contained in the filtrate.

Release of New Inbred Lines and Hybrids Resistant to Pests. Thirteen new inbred lines or varieties of cereal grains with specific resistance to certain diseases and insects were released in FY 1969 by the U.S. Department of Agriculture in cooperative Federal-State programs.

Biological Control of Alfalfa Weevil. Indications are that 5 European parasites of the alfalfa weevil introduced during the past 10 years are definitely responsible for reduced weevil populations in alfalfa fields in the Mid-Atlantic States, where most of the releases have been made. Virtually no insecticide applications were required to control the weevil in Delaware during 1969; treatments were required in only 20-30% of the fields in New Jersey and Pennsylvania. In contrast, 5 years ago, nearly all alfalfa fields in these three states required insecticide treatments to prevent crop loss.

Insect and Disease-resistant Alfalfa Germplasm Pools Released. Two pools of alfalfa germplasm, MSE-6 and MSF-6, were released cooperatively with the Nevada Agricultural Experiment Station to plant breeders. MSE-6 and MSF-6 are vigorous populations with broad genetic bases that possess resistance to the pea aphid and to biotypes ENT-A and ENT-B of the spotted alfalfa aphid. They are moderately resistant to bacterial wilt and stem nematodes. The damage that the spotted alfalfa aphid causes to alfalfa is estimated at $26 million annually. Resistant varieties save the grower $10 to $15 per acre in spray costs alone.

First Weevil Resistant Alfalfa Variety Released. Team, a newly released alfalfa variety with disease and insect resistance, promises better crops for growers in Maryland, Virginia, and North Carolina. The new variety is the first in certified seed production that has improved resistance to the alfalfa weevil, which causes yield and quality losses of some $57 million annually, exclusive of insect control costs. Team is highly resistant to the pea aphid and moderately resistant to anthracnose, *Stemphylium* leaf spot, and common leaf spot. In the mid-Atlantic area, use of Team alfalfa will reduce the need for insecticides. In Maryland, insecticide applications on this variety were not needed for control of the weevil during the past 2 years.

Sterilization of Male Boll Weevils Achieved. Busulfan, fed to adult boll weevils for 6 days as 0.1% of the diet, induced permanent and nearly complete sterility in nearly all males and caused only moderate mortality. In at least four consecutive matings, the treated males displaced normal sperm in previously mated females. The production of sex pheromone in treated males was normal.

Use of Nondiapausing Boll Weevils for Population Suppression. To survive the winter in most areas of the United States after frost has killed the cotton plants, boll weevils must be in a state of dormancy called diapause. A strain was developed in which most individuals lack the ability to diapause. In experimental field releases in Mississippi, only a small percentage of the hybrid progeny of the nondiapause and native weevils were able to survive the winter. Plans are to further evaluate the potential utility of the nondiapause strain in connection with sterile male releases.

Biological Control of Larch Casebearer is Promising. Assessment of an introduced parasite released as a bio-control agent for the larch casebearer in northern Rockies shows that the parasite has become established in 50 percent of the release plots since 1964. This combined with as much as 40 percent parasitism by native parasites looks very promising in keeping losses within tolerable limits without chemical application.

Introduced Parasite of Elm Bark Beetle Established. The parasite, Dendrosoter protuberans, imported from native haunts in Europe, is now well established in populations of its primary host, the smaller European elm bark beetle, in the Central States. In Missouri and Ohio, observed parasitism ranges from 25 to 40 percent. Three native parasites are commonly associated with the bark beetle, also. These natural enemies can be developed for use in an integrated control program to prevent Dutch elm disease build-up and spread.

TECHNOLOGY

Droplet Size Regulation. Spray generators have been developed to produce a narrow range of droplet sizes, and to capture and reclaim droplets of other sizes. This improves control of deposition on plants and reduces drift of fine droplets.

Granular Pesticide Dispenser. Dispensing of granular pesticides from hoppers can be made more uniform by design changes recently developed. Improvements in uniformity make it possible to reduce the total amount of pesticidal material required for effective pest control.

Insect-resistant Bags. The effectiveness of insect-resistant treated kraft/cotton laminated bags in protecting overseas shipments of food has been established.

Development of ULV - Short Boom Aerial Spray System. A new low cost versatile short-boom which can be installed and removed from any aircraft in less than two hours was successfully tested for ultra low volume (ULV) application against mosquitoes. This system should be very useful in emergency situations where large numbers of spray planes are needed to combat vector-borne diseases, epidemics, and insect outbreaks.

Ultra Low Volume Application. A safer yet effective pesticide application device has been developed to protect dairy animals from horn flies. The device employs the ultra-low-volume (ULV) technique and results in less quantity of pesticide required. Through use of this device and twice daily application horn flies were effectively controlled. The amount of pesticide required and correspondingly the amount of residue found in milk was reduced about a hundredfold.

New Adjustable Helicopter Spray System. A helicopter spray system for ultra-low volume application of microbial and chemical insecticides has been developed by Forest Service entomologists and engineers that allows changes in the rate of application from about 0.1 to 0.5 gallon per acre while in the air. Spray atomization remains constant if desired, or the spray spectrum can be altered by varying the spinning rate of the atomizing devices.

Careful Timing Reduces Number of Fungicide Treatments. In the Gulf States, weather favoring infection of pine nursery seedlings by fusiform rust is produced by high pressure systems. It is now possible to predict weather conditions favorable to rust infections 5 days in advance. By confining control efforts to these high-risk periods, rust losses in pine nurseries are minimized while pesticide use and costs are reduced.

New Control Methods Tested. Pilot control studies utilizing nonpersistent insecticides were conducted on 14,231 acres in Idaho and Washington. A new stabilized formulation of pyrethrum showed promise in controlling the hemlock looper. Zectran applied in very fine droplets failed to meet control criteria in suppressing the spruce budworm.

Systemic Insecticides Effective Against Cone Insects. Bidrin, Meta-Systox-R, Cygon, and Monitor applied at the rate of 5 grams active toxicant per inch of tree diameter reduced coneworm attacks in second-year slash pine cones by 80 to 90 percent. The Bidrin and Meta-Systox-R treatments reduced damage by another serious pest, the slash pine seedworm, by 95 percent. These materials are less toxic than others previously tested and found effective.

Cultural Treatment Is Improvement Over Chemical Brush Control. Following chemical brush control with 2,4-D, rabbit browsing is apt to be severe on Douglas-fir and other planted conifers. Oregon studies have indicated that where rabbits are prevalent, brush eradication by piling and burning instead of by chemicals should be considered.

Safer Rodenticide Under Test. A cooperative study is being conducted to test Diphacin as a substitute for sodium fluoroacetate to control seed-eating rodents prior to reforestation.

Improved Methods of Direct Seeding Reduces Pesticide Hazards. Previously mice and moles had been eating surface-sown seeds of white and red pine, even when coated with the rodent repellent endrin. Development of a mechanized seeder, which sows the seed and covers them with soil, resulted in very low seed losses to rodents. This makes direct seeding on rough lands practical even with very low levels of endrin. A reduced level of Arasan (1-1/2 percent) was also used on all seed in combination with the endrin.

Endrin-Arasan applications were tested to protect direct-seeded black walnuts from small mammals. Application directly to the nut, rather than to the soil proved more effective and introduced less endrin into the ecosystem.

Pest Management. Scouting programs will be inaugurated for selected crops in an attempt to reduce pesticide use by basing applications on pest counts rather than regular use for preventative control.

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Occurrence and Significance of Pesticide Residues in Water[1]

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Man throughout the civilized world is rapidly coming to realize that environmental contamination, with its harmful ecological implications, is a matter to be taken seriously. I bring to your attention one facet of environmental contamination; namely, water pollution by pesticides. It is but another example of the adage that a good thing in the wrong place can be undesirable.

The Problem

Water pollution by pesticides became a problem in the 1940's concurrently with rapid advances in pest control made possible by the development of new synthetic toxicants. Many of these synthetics are remarkably lethal to aquatic forms of life. Farmers were startled at the sudden loss of fish in their ponds and streams following rains sufficient to cause runoff from treated cropland (Young and Nicholson, 1951). Aerial applications of DDT to control forest insects were quickly followed by losses of valuable sports fish and the aquatic insects upon which they fed (Hoffman and Drooz, 1953; George, 1959).

Today we still experience periodic losses, but we know considerably more than formerly about their causes and prevention. We know that sublethal quantities of pesticides, primarily chlorinated hydrocarbon insecticides, occur widely and frequently in our streams, lakes, and even in the sea. This occurrence is indirectly evident through the recovery of residues from the tissues of fish (Nicholson, 1967; Anon., 1963), and directly evident by chemical analysis of water. In an effort to determine the extent of pesticide pollution throughout the United States, Weaver *et al.* (1965) examined water samples in September 1964 from 56 rivers and 3 of the Great Lakes. Chlorinated hydrocarbon insecticides were found in 44 rivers and in Lake Michigan at Milwaukee at concentrations ranging from 0.002 to more than 0.118 μg/liter. Dieldrin was found in 39 rivers and Lake Michigan; DDT, or its metabolite DDE, was found in 25 rivers; and endrin was found in 22 rivers and Lake Michigan.

The two principal sources of water contamination by pesticides today are runoff from the land and discharges of industrial wastes. Other causes are (a) activities intended to control aquatic life (plants, fish, or insects), (b) carelessness and accidents.

Runoff from the Land

Consider first insecticide runoff from the land. In 1959 my laboratory undertook to follow the course of water pollution by insecticides in a single large agricultural watershed over a period of nearly seven years (Nicholson *et al.*, 1966). We selected a 400-square-mile cotton-growing area in northern Alabama in which cotton acreage varied annually from 13,000 to 16,000 acres. From 8 to 84% of this acreage was treated with insecticides each summer depending upon the degree of boll weevil and bollworm infestation. The quantity of technical grade insecticides used each year varied from 12,000 to 140,000 pounds. Toxaphene, DDT, and BHC accounted for 94–99% of all usage.

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Water sampling was done nearly continuously at a municipal water treatment plant situated at the downstream end of the river basin. Thus, water samples represented drainage from the entire study area. We learned the following:

(a) Insecticides did run off the land. They entered the river from the watershed in general, rather than from a few favorably located cotton fields.

(b) Toxaphene, DDT and BHC were recovered in water samples in concentrations generally less than 1 μg/l. Highest mean recoveries were usually made during the summer, the season of application.

(c) Nearly all water samples contained insecticides year around during years of heaviest application. Toward the end of two years of minimal application (12,000 and 14,000 lbs., respectively), the frequency of negative water samples increased, indicating an improvement in river water quality with diminished insecticide usage.

(d) Toxaphene and BHC, first and third in poundage applied, were the most frequently found in water. DDT, which constituted 26–35% of the pesticides used, was recovered only during the fifth and sixth years of observation.

(e) DDT exhibited a marked affinity for sediment, and suspended sediment was the primary vehicle for its transport, thus accounting for its tendency to appear less frequently in water. Toxaphene and BHC, in contrast, were found much less frequently in association with sediment and were transported primarily in solution in the water.

A study by Bailey and Hannum (1967) reported from California sheds further light on runoff as a means of pesticide transport. Approximately 20% of all pesticides used in the United States annually is applied in California. The areas studied included the agriculturally important Imperial, San Joaquin, and Sacramento Valleys, where irrigation is required for successful farming.

Major findings were:

(a) DDT, DDD, toxaphene, heptachlor epoxide, lindane, dieldrin, and BHC were found both in surface water and in tile drainage water in concentrations generally less than 1 μg/l.

(b) All aforementioned insecticides, except BHC, were found in sediment and ranged from 1 to 1200 μg/l.

(c) Thiophosphate insecticides, which degrade more readily, were detected primarily in agricultural drainage, irrigation wastewater, and surface water directly associated with insecticide applications.

(d) Pesticide concentrations were highest in agriculturally developed areas and decrease in surface water in proportion to inflow dilution and uptake by sediment and aquatic organisms.

Manufacturing Wastes

Manufacturing wastes also may contain quantities of pesticides sufficient to have a decided impact on water quality. The types of industries involved include producers of basic pesticides, cooperage firms that reclaim used pesticide drums, and textile plants that mothproof woolen yarns and fabrics with dieldrin. These plants usually have liquid wastes requiring disposal—wastes which frequently contain residues of unrecovered pesticides.

Virtually all of these industrial plants provide some sort of waste treatment, but it is not always as effective as it should be. Dilution in the receiving stream cannot be depended upon to eliminate the impact of the waste load. Sublethal residues of chlorinated hydrocarbon insecticides can undergo a buildup in biotic components of the receiving water body, and ordinarily sublethal quantities of organophosphate pesticides may, through extended exposure, progressively inhibit the acetylcholinesterase enzyme to a degree that can kill aquatic life. Direct and catastrophic damage also has occurred when in-plant trouble resulted in an unanticipated slug discharge of wastes containing concentrations of a pesticide sufficient to be acutely toxic. An example of such a situation and its successful management follows.

A plant in Alabama which manufactures parathion and methyl parathion experienced a breakdown in its waste treatment facility in May 1961 (Anon., 1961). Process wastes were discharged to the sewerage system of an adjacent city and approximately 60% of the combined sewage and industrial waste was diverted, untreated, to a small stream during the breakdown. Fish, turtles, and snakes died along 28 miles of the stream, the average discharge of which at the time was 211 million gallons a day at a velocity of three-fourths mile per hour. The creek entered the Coosa River the average discharge of which was then about 28 times greater than that of the creek. Yet even with that dilution, parathion residues were recovered 90 miles down the Coosa and some lesser fish kills occurred in it. After a second fish kill in 1966, the company constructed a basin for temporary containment of its wastes, should another emergency arise. This simple device, along with the usually adequate waste treatment normally provided, should effectively prevent recurrence of the problems previously experienced.

Accidents and Carelessness

Perhaps the third most significant cause of pesticide pollution lies in accidents and accident's handmaiden, carelessness. Intensive educational campaigns sponsored by agricultural, conservation, water-pollution-control, and public health agencies and by the agricultural chemicals manufacturing industry have reduced the frequency of such occurrences. Most farmers have learned that it is inadvisable to dump unused spray residue where it might run into a waterway, and that they should not wash out spray equipment in a creek. Aerial applicators now pay heed to the protection of ponds and rivers. Nevertheless, some instances of water pollution by pesticides still occur as a result of thoughtlessness and accidents. An instance in which human health was at stake will serve as an example (Anon., 1964).

In 1964 a rancher instructed his hired hand to dispose of approximately fifty 4-lb. bags of over-age 15% parathion dust. Unknown to the rancher, this was done by dumping the bags off a highway bridge into the Peace River one mile upstream from the municipal water intake of Arcadia, Florida, a town of about 6,000 people. The act was discovered when some boys fishing near the bridge hooked a bag and had the foresight to report it.

The town fortunately had an auxiliary well for emergency use and immediately reverted to it. The citizens were instructed not to use the water, and flushing of the mains was begun. Subsequent analysis of water samples showed that the parathion concentration in the distribution system after flushing was generally less than 1 μg/l. However, a series of samples taken from a tap at the local bus station contained amounts up to 380 μg/l.

Investigation revealed that the bags of parathion had been dumped in the river about 10 days before their discovery. The bags were polyethylene lined and resisted rapid disintegration. Many were recovered unbroken and those that did disintegrate apparently did so intermittently over a period of several weeks. This may have been the reason that residue levels sufficiently high to be a threat to human health or the fish in the river did not occur. All but 8–12 bags were eventually found. Parathion residue occurred in river water for about two weeks after discovery at concentrations generally less than 1 μg/l.

Control of Aquatic Life

The chemical control of aquatic weeds, rough fish, and aquatic insect pests is generally managed by professionals so that undesirable consequences are minimized. A need currently exists for herbicides approved for broader use in water. A joint committee of the Departments of the Interior and Agriculture are seeking a solution to this need. A similar, but remotely related, source of pesticide residues is poaching for fish. We still have instances where insecticides, frequently toxaphene or DDT, are illegally released in water to catch fish.

Ground Water Pollution

No broad discussion of this subject would be complete without considering ground water. The potential for pesticide contamination of ground water is very much less than for surface water. However, it can occur.

A case is on record in Florida where the municipal water supply wells of a city of 25,000 contained low levels of parathion (usually less than 1 μg/l) over a several month period in 1962-63. The city's water supply consisted of both surface water, which reached the municipal water treatment plant via a canal from a citrus fruit producing area, and of five wells which were located in the vicinity of the treatment plant. The water from both sources contained parathion. The wells were rather shallow—drilled to a depth of about 100 feet and screened both at the bottom and at about the 30- to 50-foot levels. It is speculated that heavy pumping from the wells drew down surface water from the canal.

A more serious instance occurred in the South Platte River Basin near Denver, Colorado in the mid-1950's, caused by seepage of 2,4-D and related compounds from an industrial waste lagoon (Cottam, 1960). Water from wells in a 6.5-square-mile area when used for irrigation was sufficiently contaminated to cause crop damage.

Eye (1968) concluded after a study of the physical-chemical behavior of dieldrin in the soil that residues of this insecticide cannot be transported in significant amounts through soils into subsurface water by infiltration, and therefore they pose no threat to the quality of ground water. We have examined many well water samples from the Southeastern States and only in a few instances have we detected any evidence of chlorinated hydrocarbon insecticides. In those few cases, I recall only two in which direct contamination did not seem to be a possible cause. On the other hand, Bailey and Hannum (1967) in California reported recovering a broad range of chlorinated hydrocarbon insecticides~~. In those few cases I recall~~ from underground tile drains from irrigated cropland. They did not speculate on how insecticides entered the drains. A possible route might be through cracks or other direct passages from the surface.

In several of our mid-western States, where water of high quality is in limited supply, consideration is being given to using runoff water collected seasonally in playa lakes as a source from which to recharge ground water aquifers. The Robert S. Kerr Water Research Center of the Federal Water Pollution Control Administration at Ada, Oklahoma, is engaged in studies to determine the quality of recharged water, including the persistence and distribution of pesticides that may be contained in such water, after being pumped into the ground for storage.

Significance

We have seen that water contamination by pesticides occurs widely and commonly at concentrations generally less than 1 μg/l. Higher concentrations occur intermittently. But of what significance are such occurrences?

Aquatic Life

Quite clearly the unintentional killing of fish and other aquatic life by overwhelmingly lethal concentrations of pesticides is harmful and undesirable. Occurrences of this type are generally local, readily apparent, and sporadic, with partial or total repopulation quickly occurring.

Widespread, long-term, low-level contamination of the environment is much more difficult to evaluate and is a matter of growing public concern. It is caused primarily by a few compounds, members of the chlorinated hydrocarbon insecticide group—the so-called "hard" insecticides—that persist so long in nature and therefore escape our control after they are applied. Other pesticides, by and large, either degrade with reasonable rapidity or are so restricted in usage as to be of less concern except in special cases. One is tempted to speculate as to whether we would have had the public outcry over pesticides that we have experienced during the past 10 to 15 years had it not been for these few "hard" insecticides. I am inclined to think that it would have been much less extensive.

The single sublethal manifestation with chlorinated hydrocarbons that is most obvious, and the significance of which is least understood, is that of biological accumulation. Biological accumulation may occur through direct absorption from the water or by absorption and passage through the food chain. The implications for damage are great, but well defined examples of proved harm are few, perhaps because biological accumulation is not as generally damaging as feared, but also perhaps because the ecological relationships involved are so extremely complex that they are difficult to unravel.

Light has been cast on this phenomenon by numerous researchers. Cope (1965), investigating the distribution of DDT through various compartments of a simplified ecosystem, reported that two weeks after the application of ^{14}C–DDT at a concentration of 20 μg/l to aquarium water, the water contained 0.42 μg/l, soil contained 6 μg/kg, and vegetation contained 15,600 μg/kg. Two weeks after fish were placed into the aquaria, they contained 1,000 μg/kg of DDT. Woodwell *et al.* (1967) investigated biological concentration of DDT among various trophic levels of a Long Island salt marsh and reported values increasing from 0.04 mg/kg in plankton to 75 mg/kg in ring-billed gulls. Highest concentrations occurred in scavenging and carnivorous fish and birds, although the birds had 10–100 times more than the fish. Gakstatter and Weiss (1967) exposed bluegills and goldfish in aquaria to ^{14}C–DDT, dieldrin, and lindane to study uptake, retention, and release by the fish. They showed that the lindane was entirely released within two days and that more than 90% of the initial dieldrin was eliminated within two weeks. However, more than 50% of the DDT was still retained after 32 days. More significant, they showed that DDT and dieldrin were readily transferred from contaminated to uncontaminated fish held in clean water. Apparently, some of the persistent insecticides are capable not only of undergoing biological magnification but also of cycling between water and the organisms living in it.

The accumulation of pesticides in the bodies of fish has been cited as the probable cause of the secondary poisoning of a variety of fish-eating birds. The most notable example is that described by Hunt and Bischoff (1960) in which western grebes overwintering on Clear Lake, California died, presumably from eating fish containing high DDD residues. Keith (1966) reported an unusually high mortality of fish-eating birds between 1960 and 1962 at the Tule Lake National Wildlife Refuge in California, which he attributed, circumstantially, to ingestion of toxaphene accumulated in fish. A study of this refuge in 1965–66 (Godsil and Johnson, 1968), when endrin was the principal insecticide used on the nearby irrigated farmland, indicated a marked increase of endrin in all trophic levels during the crop-growing season (May-Sept.) with a subsequent decline to near or below detectable limits in the off season. Fish accumulated maxima of 97 μg/kg in 1965 and 107 μg/kg in 1966. Endrin was not established as a permanent residue, and no wildlife losses were recorded. It is apparent that the so-called "hard" insecticides are not equally accumulative or persistent in food chain compartments.

Butler (1966 a, b, c) has done extensive work on the effects of low levels of chlorinated hydrocarbon insecticides on organisms of the marine environment. He showed that DDT in the water at levels as low as 1 μg/l caused a 20% reduction in oyster growth, and that oysters are efficient concentrators of DDT in their tissues. He believes that pesticides may be the cause of ill-defined but significant mortality, loss of production, and perhaps changes in the direction of natural selection in estuarine fauna. Cope (1965) concluded that exposure to sublethal amounts of DDT increases fish mortality by reducing resistance to other stresses.

Burdick and his co-workers (1964) in New York demonstrated that lethal amounts of DDT can be transmitted from female lake trout to their offspring through the egg. Lethality bore no relation to the concentration of DDT in the female. Fry died when the final contents of the yolk sacs were absorbed. These deaths occurred when the eggs contained DDT equivalent to 2.9 mg/kg or more of fry. This situation came to light when complete loss of lake trout fry occurred in 1955 and 1956 at a Lake George fish hatchery. It is a most subtle adverse effect that would be detected only under hatchery or laboratory conditions.

The influence upon the survival of aquatic organisms of transovarially conveyed pesticide residues is a subject worthy of further research. The period of dependence upon food stored in the egg sac may be for numerous fish species the most vulnerable period in their life histories as far as pesticides are concerned. If this is true, the chances are very slight that population losses would be directly observed in nature short of virtual elimination of a major species.

Much has been written about the effects of long-term exposure of aquatic organisms to pesticides at sublethal levels, but we still have a remarkably small amount of compellingly positive information indicating danger from organic chlorinated insecticides. DDT has received by far the most attention, possibly because its residues are so universally distributed. We need more research on other persistent insecticides. Although we do not have agreement within the scientific community concerning the danger of persistent residues in living organisms and in the environment, perhaps all can agree that it would be better if we did not have these uncontrolled residues.

Other Water Uses

In April 1968 the National Technical Advisory Committee on Water Quality Criteria of the Federal Water Pollution Control Administration submitted its first report to the Secretary of the Interior (Anon., 1968). This volume constitutes the most comprehensive document to date on water quality requirements for various uses. It contains recommendations for permissible limits for some pesticides.

The Subcommittee on Public Water Supplies based its recommendations on pesticides upon recommendations submitted by the Public Health Service Advisory Committee on Use of the Public Health Service Drinking Water Standards. The values were derived for that committee by an expert group of toxicologists and were established at those levels which, if ingested over extensive periods, could not cause harmful or adverse physiological changes in man. In the case of aldrin, heptachlor, chlordane, and parathion the values were set even lower than those physiologically safe, to avoid levels that could be tasted or smelled. Table 1 contains these recommendations.

Table 1. Surface Water Criteria for Pesticides in Public Water supplies (mg/l).[1]

	Permissible criteria	Desirable criteria
Aldrin	0.017	Absent
Chlordane	0.003	"
DDT	0.042	"
Dieldrin	0.017	"
Endrin	0.001	"
Heptachlor	0.018	"
Heptachlor epoxide	0.018	"
Lindane	0.056	"
Methoxychlor	0.035	"
Organic phosphates plus carbamates	0.1[2]	"
Toxaphene	0.005	"
2,4-D plus 2,4,5-T, plus 2,4,5-TP	0.1	"

[1] Adapted from Water Quality Criteria, Report of the National Technical Advisory Committee to the Secretary of the Interior, April 1968. Washington, D. C.

[2] As parathion in cholinesterase inhibition. It may be necessary to resort to even lower concentrations for some compounds or mixtures.

The subcommittees concerned with criteria for aquatic and wildlife (both freshwater and marine) and for agriculture each considered pesticides. The criteria, or formulae for determining criteria values, are generally too complex to justify discussion here, and the reader is referred to the original source.

An alternative suggestion for a water-quality criterion for fish, based on a group effect of about 100 organophosphorus and carbamate compounds, was derived at the Southeast Water Laboratory (Nicholson, 1967). This practical suggestion was based upon the ability of these compounds to inhibit acetyl-cholinesterase activity in the brains of fish. The degree of inhibition is a function of the compound, its concentration in water, and the duration of exposure. Death results from inhibition ranging from 40 to 70%. As little as 10% inhibition can be measured and statistically confirmed in a group of ten fish of the same species and of similar size. Therefore, it was suggested that 10% acetylcholinesterase inhibition in fish brain would serve as a good criterion of water quality involving chemicals capable of causing this inhibition. Unfortunately, no group effect for organochlorine insecticides has yet been developed upon which a similar criterion can be established.

Pesticide Pollution Control

The Southeast Water Laboratory has national responsibility within the Federal Water Pollution Control Administration for research leading to the control of pesticide pollution. Control is generally easiest at point sources; i.e., at industrial sources where waste effluent is discharged to a stream at a single outfall. We are currently beginning an inventory of waste-treatment practices at pesticide manufacturing and pesticide using industrial plants to establish a mutually beneficial relationship with some of these industries. Control may be accomplished by a variety of waste-treatment processes and by in-plant process changes. Effective control may be as simple as the provision of facilities for biochemical oxidation of effluents with auxiliary provision of a basin for containing extraordinary peak loads of wastes for more leisurely disposal. Our Laboratory is equipped with a variety of advanced analytical instruments, including a 100-megacycle high-resolution nuclear magnetic resonance spectrometer and a computerized mass spectrometer, with which we are able to determine the chemical nature of industrial waste effluents and assist in optimizing the design of advanced waste treatment systems.

The control of pesticide pollution associated with rural runoff is much more difficult to accomplish because its entrance into watercourses is not localized. Therefore, control must be accomplished by other means and ultimately rests in the hands of the users. Land-management practices designed to retard water runoff and soil erosion certainly are helpful measures. The retention of an untreated buffer strip adjacent to mountain streams was shown to prevent the runoff of DDT ap-

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plied for forest insect control (Grzenda *et al.*, 1964).

We are conducting research with pure clay mineral model soils to develop basic concepts relative to the retention of representative pesticides on the land or their failure to be retained. Recently our scientists, cooperating with associates at Purdue University, demonstrated that s-triazine herbicides may be irreversibly adsorbed onto montmorillonite clay, and in so doing, undergo a chemical change to an innocuous compound (Russell *et al.*, 1968). Basic concepts developed are later confirmed with natural soils. The results frequently are directly applicable to rural runoff control recommendations.

Pesticide runoff from the land is directly related to runoff losses of both water and surface soil: they serve to transport pesticides from farm or forest to watercourses. Controlling this process are climatic, edaphic, hydrologic, physiographic, and cultural factors. If we knew more about the interplay of soil type, slope of the land, rainfall and other climatic factors, cropping practices, and the behavior of the pesticides in use, we should be able to recommend measures to reduce the importance of rural runoff as a source of water pollution by pesticides. These recommendations might simply concern which pesticides to use or not to use in a given combination of circumstances. It might develop into water-pollution-control recommendations for geographic zones.

A comparable development has already been made in agriculture. I refer to the universal soil-loss equation that is applicable to guiding conservation farm planning throughout the United States (Wischmeier *et al.*, 1958; Wischmeier, 1969; Wischmeier and Smith, 1960, 1965). The factors upon which this equation is based are rainfall, soil-erodibility, slope length and gradient, cropping management, and erosion control practices. The possibility of extending the universal soil-loss equation and applying it to the prediction and control of pesticide pollution associated with rural runoff seems good and is being explored.

In the meantime, socio-economic developments are occurring outside the field of water pollution control that tend toward reduction of the water pollutional impact of the persistent organochlorine insecticides. The development of resistance to insecticides among cotton, corn, and sugarcane pests, to name a few, has forced total or partial abandonment of the formerly preferred "hard" insecticides in favor of more effective and, incidentally, less persistent types. Food and Drug Administration-controlled tolerance levels have required other changes. There is a growing public interest in environmental contamination control that may bring forth legislation outlawing the use of the "hard" insecticides as "hard" detergents were outlawed a few years ago. I should not like to see this happen, but would prefer to see substitutes used whenever it is feasible to do so, retaining the troublesome insecticides for use where they are absolutely necessary and where their usage will not result in further environmental contamination.

It is the responsibility of entomologists and leaders in the field of pesticide usage to take note, to look beyond the immediate problem of controlling insects, and to assume greater responsibility for preventing undesirable side effects resulting from the use of pesticides.

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